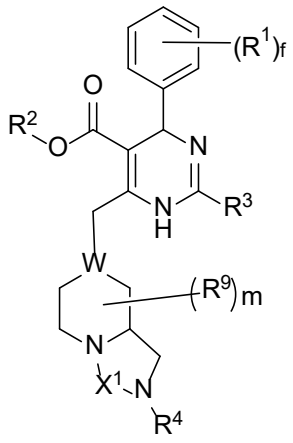
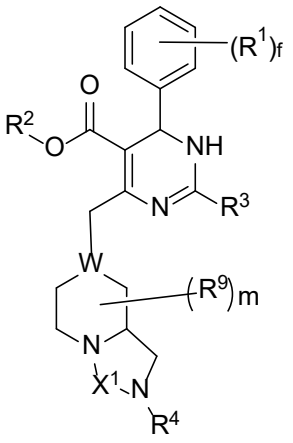
What is claimed is:

1. A compound having Formula (I) or Formula (Ia), or a stereoisomer, a tautomer, an *N*-oxide, a solvate, a metabolite, a pharmaceutically acceptable salt or a prodrug thereof,



(I) or



(Ia),

wherein each R^1 is independently H, deuterium, F, Cl, Br, I, methyl, or ethyl;

each R^2 is independently C_{1-6} alkyl, deuterium substituted C_{1-6} alkyl or C_{1-6} haloalkyl;

each R^3 is independently 5 membered heteroaryl, wherein each of 5 membered heteroaryl is independently unsubstituted or substituted with one or two substituents independently selected from deuterium, F, Cl, Br or C_{1-6} alkyl;

each W is N;

each X^1 is independently -C(=O)- ;

each R^7 and R^8 is independently H, deuterium, F, Cl, Br, amino, C_{1-6} alkyl, $NH_2C(=O)$-, C_{1-6} alkyl-OC(=O)-, carboxy, carboxy C_{1-6} alkylene, hydroxy C_{1-6} alkyl, C_{1-4} alkoxy-C_{1-4} alkyl or C_{1-6} haloalkyl, or R^7 and R^8, together with the carbon atom to which they are attached, form C_{3-6} cycloalkyl or carbonyl;

each R^9 is independently H, deuterium, C_{1-6} alkyl, $NH_2C(=O)$-, C_{1-6} alkyl-OC(=O)-, carboxy, hydroxy C_{1-6} alkyl or C_{1-4} alkoxy-C_{1-4} alkyl;

R^4 is pyridyl, 5 membered monocyclic heteroaryl, phenyl, naphthyl or phenyl-(CR^7R^8)-, wherein the 5 membered monocyclic heteroaryland naphthyl are each independently unsubstituted or substituted with one, two or three R^w, the pyridyl, phenyl and phenyl of phenyl-(CR^7R^8)- are each independently substituted with one, two, three or four R^x;

each R^w is independently deuterium, F, Cl, Br, OH, CN, $R^aR^bNC(=O)$-, $R^cR^dP(=O)$-, HOOC-$(CR^7R^8)_k$-, amino, C_{1-8} alkyl, C_{2-8} alkenyl, hydroxy C_{1-8} alkyl, C_{1-8} alkyl-C(=O)-, C_{1-8} alkoxy, C_{1-8} alkyl-OC(=O)- or C_{1-8} alkyl-$S(=O)_2$-, wherein the amino, C_{1-8} alkyl, C_{2-8} alkenyl, hydroxy C_{1-8} alkyl, C_{1-8} alkyl-C(=O)-, C_{1-8} alkoxy, C_{1-8} alkyl-OC(=O)- and C_{1-8} alkyl-$S(=O)_2$- are each independently unsubstituted or substituted with one, two, three, four or five R^y;

each R^x is independently deuterium, F, Cl, Br, OH, CN, $R^aR^bNC(=O)$-, $R^cR^dP(=O)$-, HOOC-$(CR^7R^8)_n$-, amino, C_{1-8} alkyl, C_{2-8} alkenyl, hydroxy C_{1-8} alkyl, C_{1-8} alkyl-C(=O)-, C_{1-8} alkoxy, C_{1-8} alkyl-OC(=O)-, HOOC-methylene-O-methylene-, C_{1-4} alkyl-OC(=O)-methylene-O-methylene, C_{1-4} alkyl-C(=O)O-methylene or C_{1-8} alkyl-$S(=O)_2$-, wherein the amino, C_{1-8} alkyl, C_{2-8} alkenyl, hydroxy C_{1-8} alkyl, C_{1-8} alkyl-C(=O)-, C_{1-8} alkoxy, C_{1-8} alkyl-OC(=O)-, HOOC-methylene-O-methylene-, C_{1-4} alkyl-OC(=O)-methylene-O-methylene, C_{1-4} alkyl-C(=O)O-methylene and C_{1-8} alkyl-$S(=O)_2$- are each independently unsubstituted or substituted with one, two, three, four or five R^y;

each R^y is independently deuterium, F, Cl, Br, OH, CN, $R^aR^bNC(=O)$-, $R^cR^dP(=O)$-, HOOC-$(CR^7R^8)_h$-, amino, C_{1-6} alkyl-$S(=O)_2$-NH-, C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkyl-$S(=O)_2$-, C_{1-8} alkyl-C(=O)-, C_{1-8} alkyl-OC(=O)-, benzyl-OC(=O)- or C_{1-8} alkylamino-$S(=O)_2$-, wherein the amino, C_{1-6} alkyl-$S(=O)_2$-NH-, C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkyl-$S(=O)_2$-, C_{1-8} alkyl-C(=O)-, C_{1-8} alkyl-OC(=O)-, benzyl-OC(=O)-, phenyl-OC(=O)- and C_{1-8} alkylamino-$S(=O)_2$- are each independently unsubstituted or substituted with one, two, three, four or five substituents

selected from deuterium, F, Cl, Br, OH, C_{1-8} alkoxy, C_{1-8} alkyl, HOOC-$(CR^7R^8)_h$- or C_{1-8} alkoxy-$(CR^7R^8)_n$-O-;

each R^a, R^b, R^c and R^d is independently H, deuterium, HOOC-$(CR^7R^8)_q$-, C_{1-8} alkyl, C_{1-8} alkyl-OC(=O)-, C_{1-8} alkoxy, C_{3-7} cycloalkyl or 3-12 membered heterocyclyl, wherein the C_{1-8} alkyl, C_{1-8} alkyl-OC(=O)-, C_{1-8} alkoxy, C_{3-7} cycloalkyl and 3-12 membered heterocyclyl are each independently unsubstituted or substituted with one, two, three, four or five substituents selected from deuterium, F, Cl, Br, OH, amino, C_{1-8} alkyl, C_{1-8} alkoxy, HOOC-$(CR^7R^8)_q$- or C_{1-8} alkoxy-$(CR^7R^8)_n$-O-;

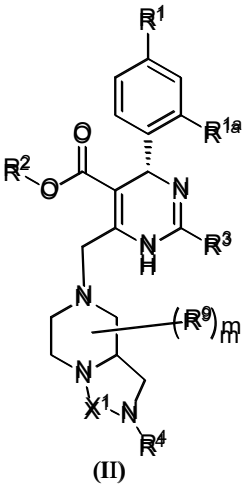
each f, k, h and q is independently 0, 1, 2, 3 or 4;

each m is independently 0, 1 or 2;

each n is independently 1, 2, 3 or 4;

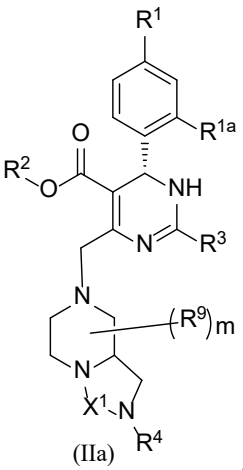
each j is independently 1, 2 or 3.

2. The compound of claim 1 having Formula (II) or Formula (IIa),



(II)

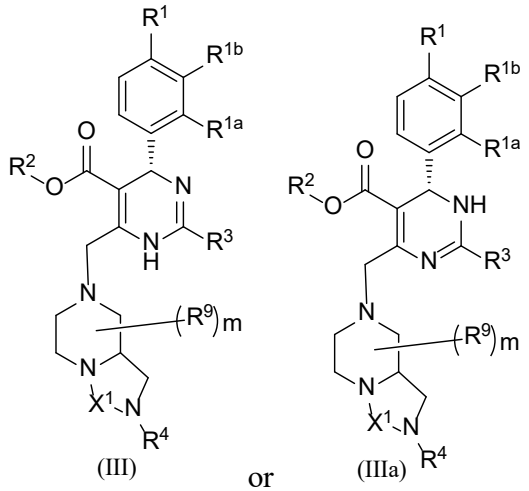
or



(IIa) ,

wherein each R^1 and R^{1a} is independently H, deuterium, F, Cl, Br, I or methyl or ethyl.

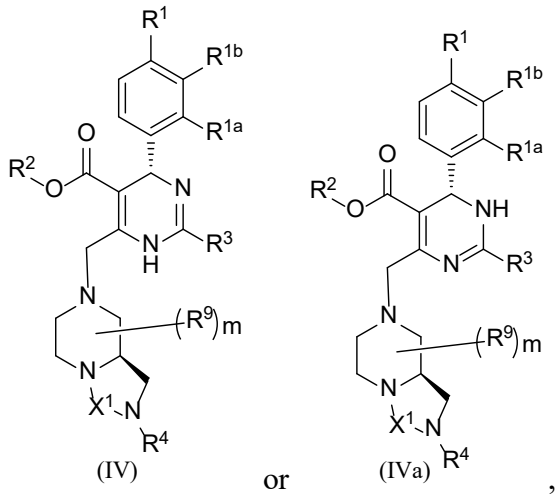
3. The compound of claim 1 having Formula (III) or Formula (IIIa),



(III) or (IIIa)

wherein each R^1, R^{1b} and R^{1a} is independently H, deuterium, F, Cl, Br, I, methyl or ethyl.

4. The compound of claim 1 having Formula (IV) or (IVa):



(IV) or (IVa) ,

wherein each R^1, R^{1b} and R^{1a} is independently H, deuterium, F, Cl, Br, I, methyl or ethyl.

5. The compound of claim 1, wherein each R^2 is independently methyl, deuterated methyl, ethyl, *n*-propyl, *i*-propyl or C_{1-4} haloalkyl;

R^3 is furyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxazolyl, oxadiazolyl, thiazolyl or thienyl, wherein each of furyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxazolyl, oxadiazolyl, thiazolyl, thienyl is independently unsubstituted or substituted with one or two substituents independently selected from deuterium, F, Cl, Br or C_{1-4} alkyl;

each R^7 and R^8 is independently H, deuterium, F, Cl, Br, methyl, ethyl, *n*-propyl, *i*-propyl, $NH_2C(=O)$-, C_{1-4} alkyl-OC(=O)-, carboxy, carboxy C_{1-3} alkylene, hydroxy C_{1-4} alkyl, ethoxyethyl, methoxyethyl, isopropoxymethyl, methoxymethyl or C_{1-4} haloalkyl, or R^7 and R^8, together with the carbon atom to which they are attached, form cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or carbonyl;

each R^9 is independently H, deuterium, methyl, ethyl, *n*-propyl, *i*-propyl, $NH_2C(=O)$-, C_{1-4} alkyl-OC(=O)-, carboxy, hydroxy C_{1-4} alkyl, ethoxyethyl, methoxyethyl, isopropoxymethyl or methoxymethyl.

6. The compound of claim 1, wherein R^4 is pyridyl, 5 membered monocyclic heteroaryl, phenyl, naphthyl or phenyl-(CR^7R^8)-, wherein the 5 membered monocyclic heteroaryl and naphthyl are each independently unsubstituted or substituted with one, two or three R^w, the pyridyl, phenyl and phenyl of phenyl-(CR^7R^8)- are each independently substituted with one, two, three or four R^x.

7. The compound of claim 1, wherein R^4 is pyridyl, furyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, thiazolyl, thienyl, phenyl, naphthyl or phenyl-(CR^7R^8)-,wherein each of furyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, thiazolyl, thienyland naphthyl is independently unsubstituted or substituted with one, two or three R^w; the pyridyl, phenyl and phenyl of phenyl-(CR^7R^8)- are each independently substituted with one, two, three or four R^x.

8. The compound of claim 1, wherein each R^w is independently deuterium, F, Cl, Br, OH, CN, $R^aR^bNC(=O)$-, $R^cR^dP(=O)$-, HOOC-$(CR^7R^8)_k$-, amino, C_{1-6} alkyl, C_{2-6} alkenyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyl-C(=O)-, C_{1-6} alkoxy, C_{1-6} alkyl-OC(=O)- or C_{1-6} alkyl-$S(=O)_2$-, wherein the amino, C_{1-6} alkyl, C_{2-6} alkenyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyl-C(=O)-, C_{1-6} alkoxy, C_{1-6} alkyl-OC(=O)- and C_{1-6} alkyl-$S(=O)_2$- are each independently unsubstituted or substituted with one, two, three, four or five R^y;

each R^x is independently deuterium, F, Cl, Br, OH, CN, $R^aR^bNC(=O)$-, $R^cR^dP(=O)$-, HOOC-$(CR^7R^8)_n$-, amino, C_{1-6} alkyl, C_{2-6} alkenyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyl-C(=O)-, C_{1-6} alkoxy, C_{1-6} alkyl-OC(=O)-, HOOC-methylene-O-methylene-, C_{1-4} alkyl-OC(=O)-methylene-O-methylene, C_{1-4} alkyl-C(=O)O-methylene or C_{1-6} alkyl-$S(=O)_2$-, wherein the amino, C_{1-6} alkyl, C_{2-6} alkenyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyl-C(=O)-, C_{1-6} alkoxy, C_{1-6} alkyl-OC(=O)-, HOOC-methylene-O-methylene-, C_{1-4} alkyl-OC(=O)-methylene-O-methylene, C_{1-4} alkyl-C(=O)O-methylene and C_{1-6} alkyl-$S(=O)_2$- are each independently unsubstituted or substituted with one, two, three, four or five R^y.

9. The compound of claim 1, wherein each R^w is independently deuterium, F, Cl, Br, OH, CN, $R^aR^bNC(=O)$-, $R^cR^dP(=O)$-, HOOC-$(CR^7R^8)_k$-, amino, C_{1-4} alkyl, vinyl, propenyl, allyl, hydroxy C_{1-4} alkyl, C_{1-4} alkyl-C(=O)-, C_{1-4} alkoxy, C_{1-4} alkyl-OC(=O)- or C_{1-4} alkyl-$S(=O)_2$-, wherein the amino, C_{1-4} alkyl, vinyl, propenyl, allyl, hydroxy C_{1-4} alkyl, C_{1-4} alkyl-C(=O)-, C_{1-4} alkoxy, C_{1-4} alkyl-OC(=O)- and C_{1-4} alkyl-$S(=O)_2$- are each independently unsubstituted or substituted with one, two, three, four or five R^y;

each R^x is independently deuterium, F, Cl, Br, OH, CN, $R^aR^bNC(=O)$-, $R^cR^dP(=O)$-, HOOC-$(CR^7R^8)_n$-, amino, C_{1-4} alkyl, vinyl, propenyl, allyl, hydroxy C_{1-4} alkyl, C_{1-4} alkyl-C(=O)-, C_{1-4} alkoxy, C_{1-4} alkyl-OC(=O)-, HOOC-methylene-O-methylene-, methyl-OC(=O)-methylene-O-methylene, ethyl-OC(=O)-methylene-O-methylene, methyl-C(=O)O-methylene or C_{1-4} alkyl-$S(=O)_2$-, wherein the amino, C_{1-4} alkyl, hydroxy C_{1-4} alkyl, vinyl, propenyl, allyl, C_{1-4} alkyl-C(=O)-, C_{1-4} alkoxy, C_{1-4} alkyl-OC(=O)-, HOOC-methylene-O-methylene-, methyl-OC(=O)-methylene-O-methylene, ethyl-OC(=O)-methylene-O-methylene, methyl-C(=O)O-methylene and C_{1-4} alkyl-$S(=O)_2$- are each independently unsubstituted or substituted with one, two, three, four or five R^y.

10. The compound of claim 1, wherein each R^y is independently deuterium, F, Cl, Br, OH, CN, $R^aR^bNC(=O)$-, $R^cR^dP(=O)$-, HOOC-$(CR^7R^8)_h$-, amino, C_{1-4} alkyl-$S(=O)_2$-NH-, C_{1-6}

alkyl, C_{1-6} alkoxy, C_{1-6} alkyl-S(=O)$_2$-, C_{1-6} alkyl-C(=O)-, C_{1-6} alkyl-OC(=O)-, benzyl-OC(=O)- or C_{1-6} alkylamino-S(=O)$_2$-, wherein the amino, C_{1-4} alkyl-S(=O)$_2$-NH-, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkyl-S(=O)$_2$-, C_{1-6} alkyl-C(=O)-, C_{1-6} alkyl-OC(=O)-, benzyl-OC(=O)-, phenyl-OC(=O)- and C_{1-6} alkylamino-S(=O)$_2$- are each independently unsubstituted or substituted with one, two, three, four or five substituents selected from deuterium, F, Cl, Br, OH, C_{1-6} alkoxy, C_{1-6} alkyl, HOOC-$(CR^7R^8)_h$- or C_{1-6} alkoxy-$(CR^7R^8)_n$-O-;

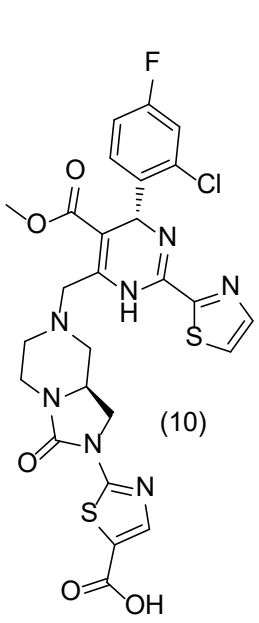
each R^a, R^b, R^c and R^d is independently H, deuterium, HOOC-$(CR^7R^8)_q$-, C_{1-6} alkyl, C_{1-6} alkyl-OC(=O)-, C_{1-6} alkoxy, C_{3-6} cycloalkyl or 5-10 membered heterocyclyl, wherein the C_{1-6} alkyl, C_{1-6} alkyl-OC(=O)-, C_{1-6} alkoxy, C_{3-6} cycloalkyl and 5-10 membered heterocyclyl are each independently unsubstituted or substituted with one, two, three, four or five substituents selected from deuterium, F, Cl, Br, OH, amino, C_{1-6} alkyl, C_{1-6} alkoxy, HOOC-$(CR^7R^8)_q$- or C_{1-6} alkoxy-$(CR^7R^8)_n$-O-.

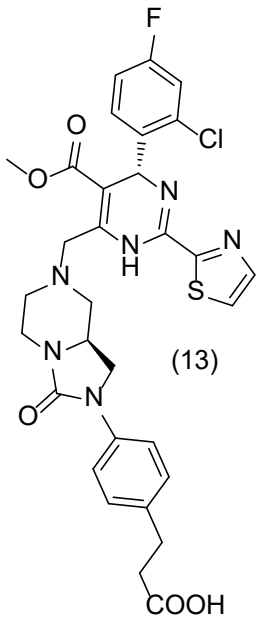
11. The compound of claim 1, wherein each R^y is independently deuterium, F, Cl, Br, OH, CN, $R^aR^bNC(=O)$-, $R^cR^dP(=O)$-, HOOC-$(CR^7R^8)_h$-, amino, methyl-S(=O)$_2$-NH-, ethyl-S(=O)$_2$-NH-, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkyl-S(=O)$_2$-, C_{1-4} alkyl-C(=O)-, C_{1-4} alkyl-OC(=O)-, benzyl-OC(=O)- or C_{1-4} alkylamino-S(=O)$_2$-, wherein the amino, methyl-S(=O)$_2$-NH-, ethyl-S(=O)$_2$-NH-, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkyl-S(=O)$_2$-, C_{1-4} alkyl-C(=O)-, C_{1-4} alkyl-OC(=O)-, benzyl-OC(=O)-, phenyl-OC(=O)- and C_{1-4} alkylamino-S(=O)$_2$- are each independently unsubstituted or substituted with one, two, three, four or five substituents selected from deuterium, F, Cl, Br, OH, C_{1-4} alkoxy, C_{1-4} alkyl, HOOC-$(CR^7R^8)_h$- or C_{1-4} alkoxy-$(CR^7R^8)_n$-O-;

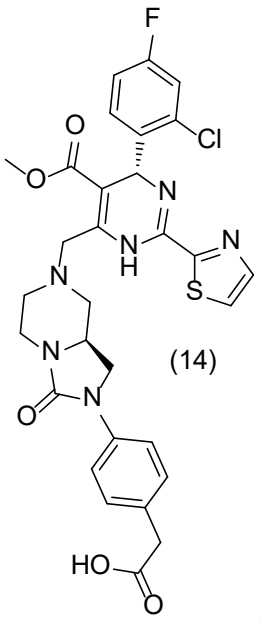
each R^a, R^b, R^c and R^d is independently H, deuterium, HOOC-$(CR^7R^8)_q$-, C_{1-4} alkyl, C_{1-4} alkyl-OC(=O)-, C_{1-4} alkoxy, C_{3-6} cycloalkyl or 5-6 membered heterocyclyl, wherein the C_{1-4} alkyl, C_{1-4} alkyl-OC(=O)-, C_{1-4} alkoxy, C_{3-6} cycloalkyl and 5-6 membered heterocyclyl are each independently unsubstituted or substituted with one, two, three, four or five substituents

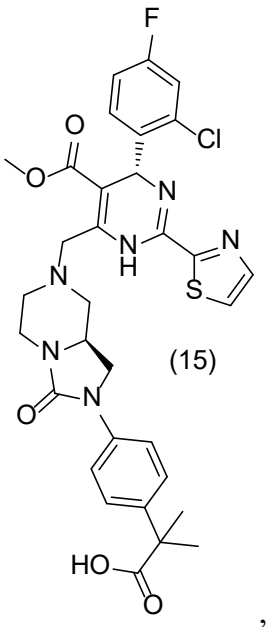
selected from deuterium, F, Cl, Br, OH, amino, C_{1-4} alkyl, C_{1-4} alkoxy, HOOC-$(CR^7R^8)_q$- or C_{1-4} alkoxy-$(CR^7R^8)_n$-O-.

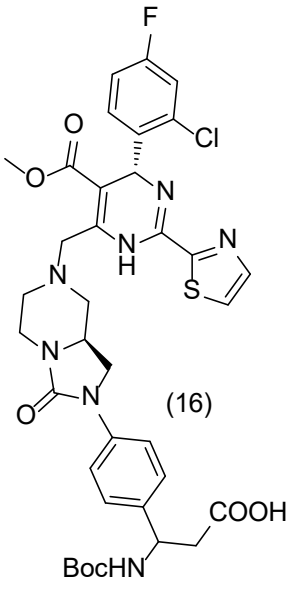
12. A compound having one of the following structures:

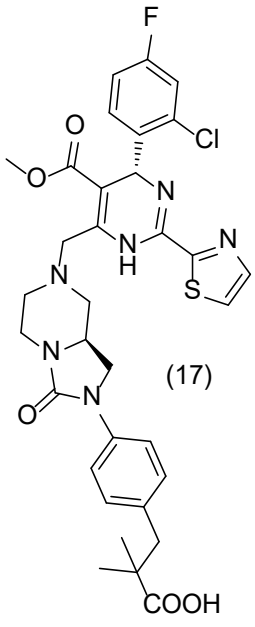

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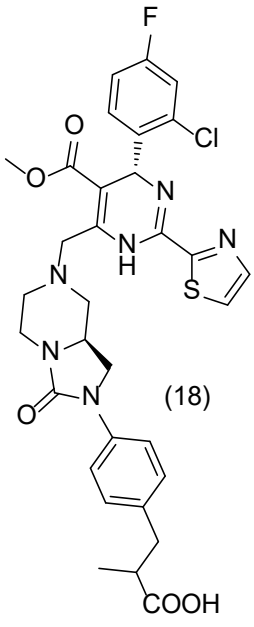

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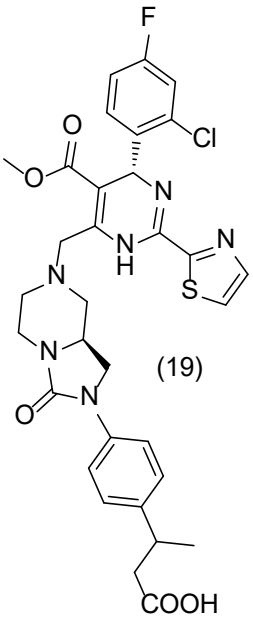

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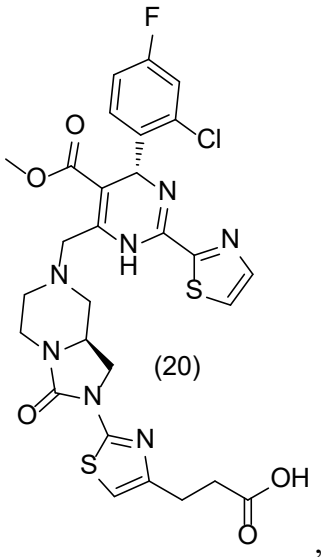
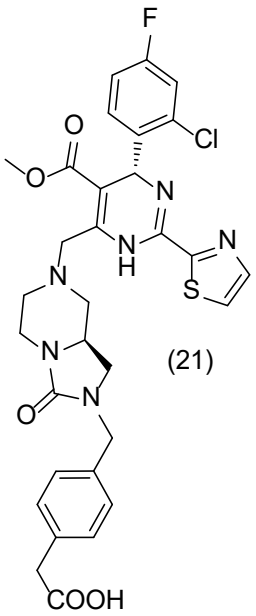
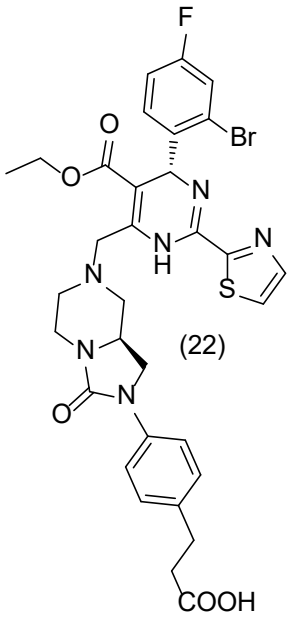
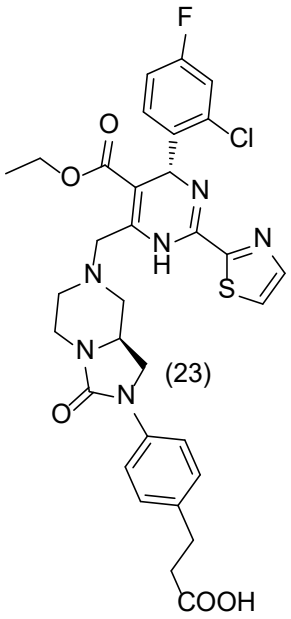
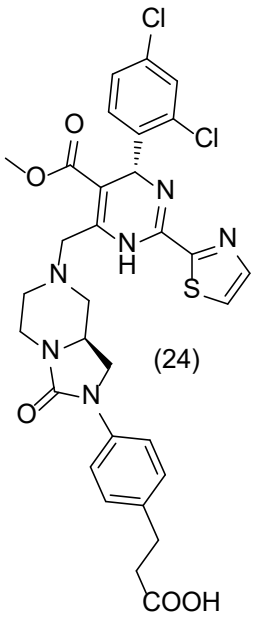
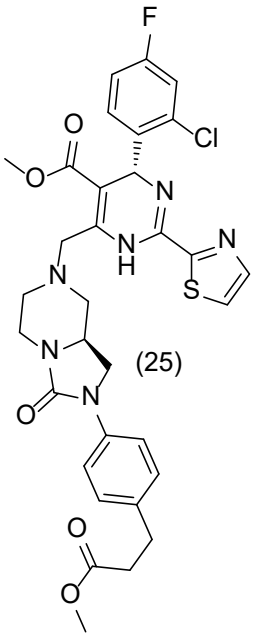
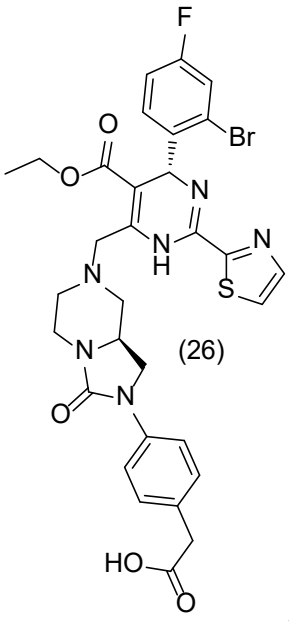

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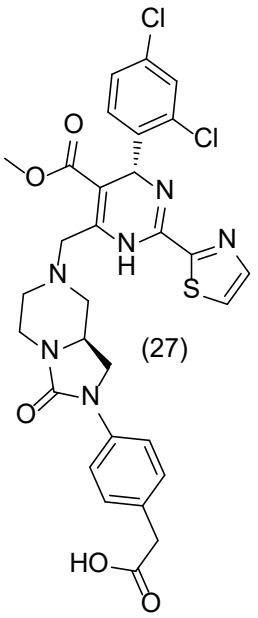
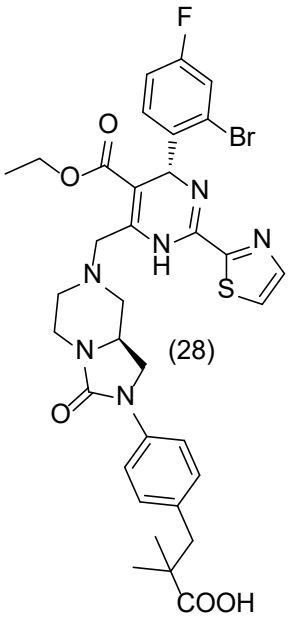
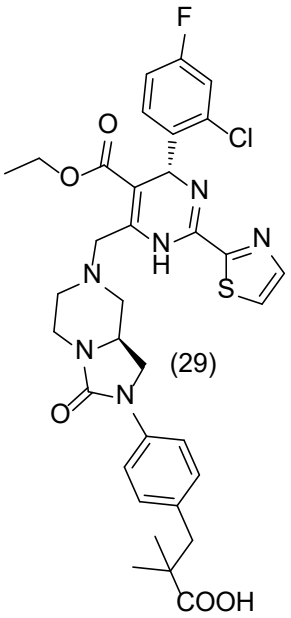
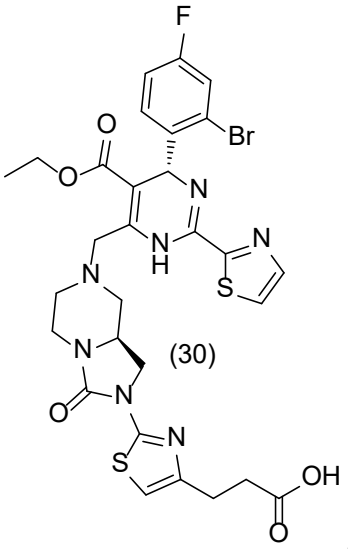
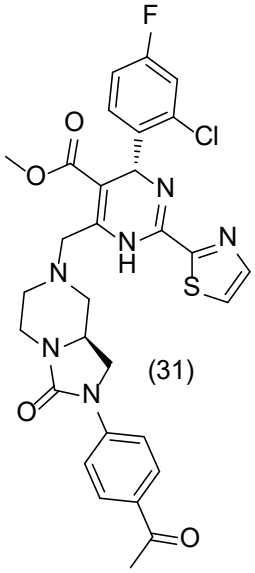
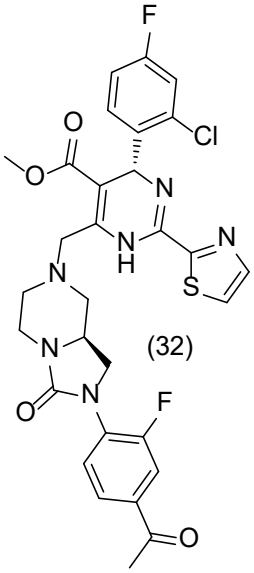
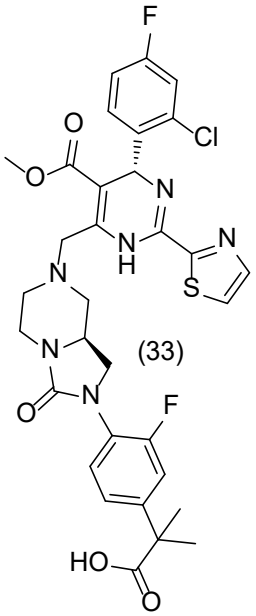

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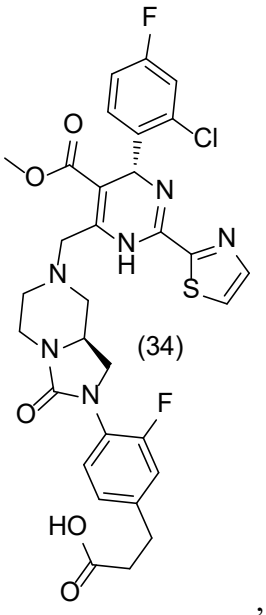
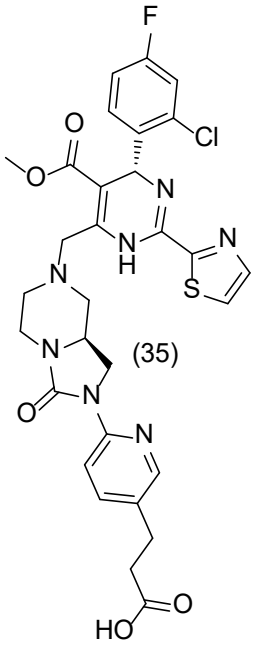
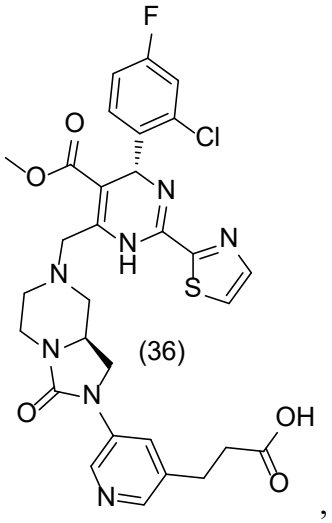
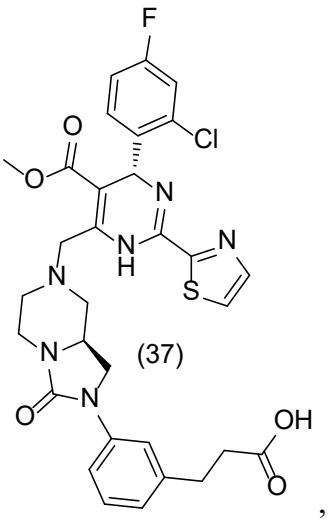
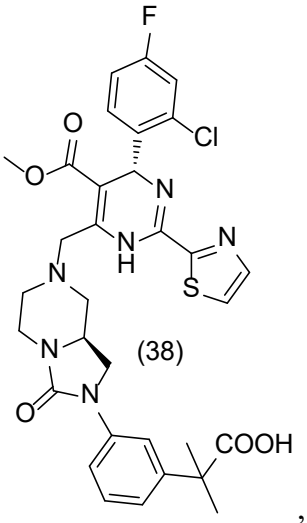
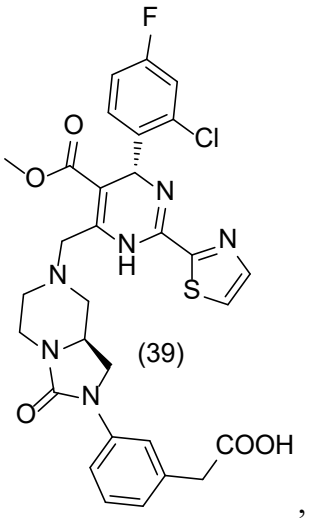
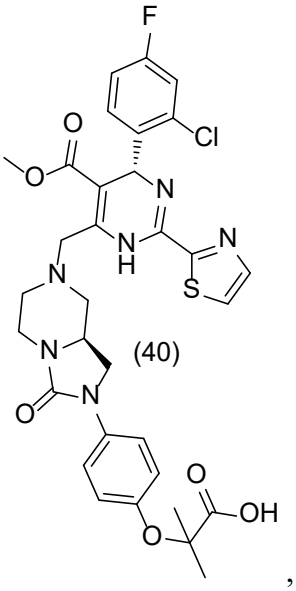
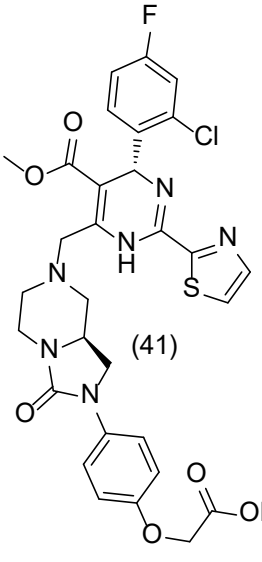
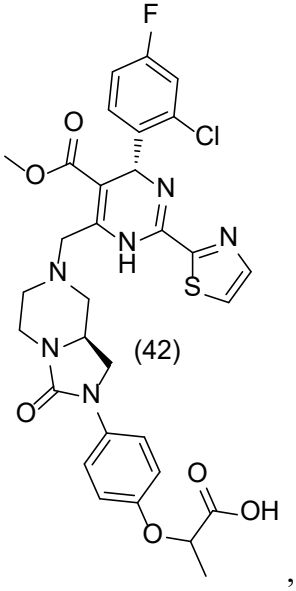

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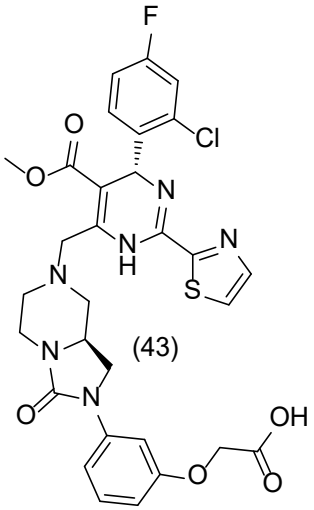
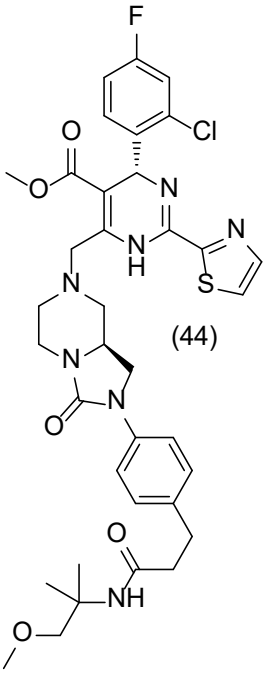
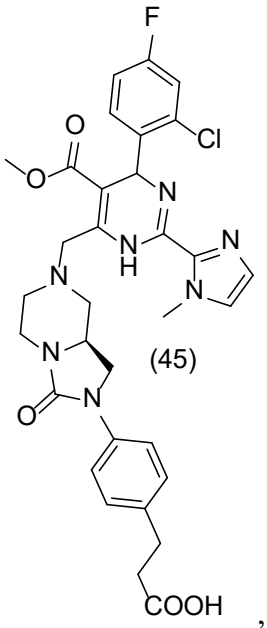
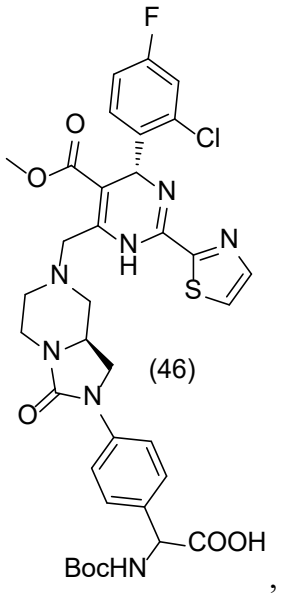
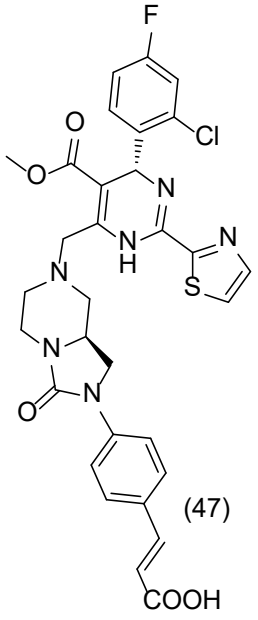
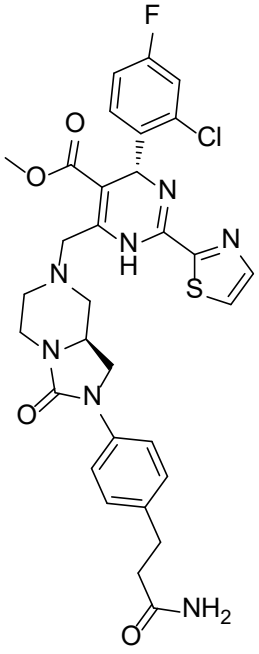
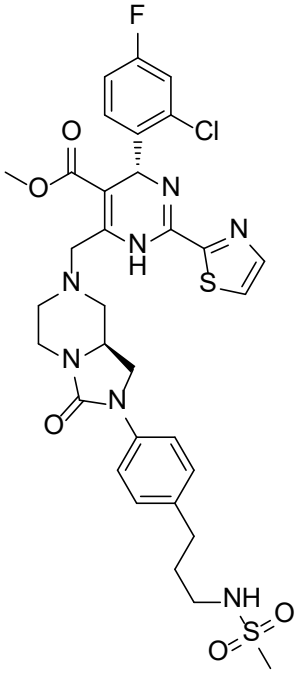

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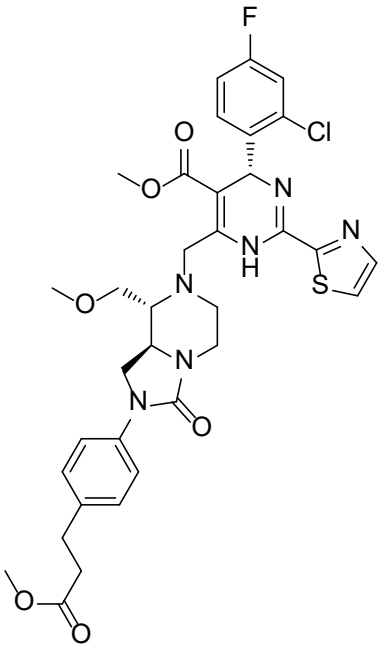

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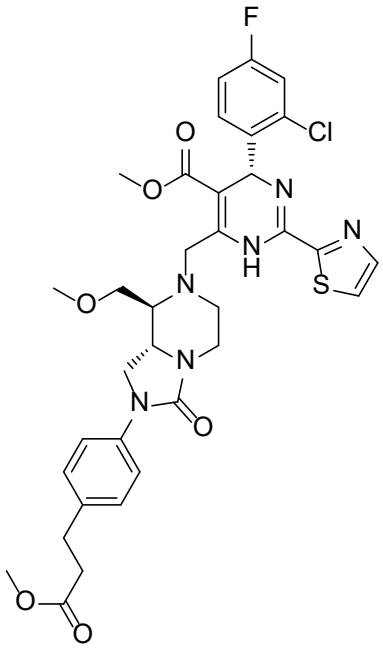

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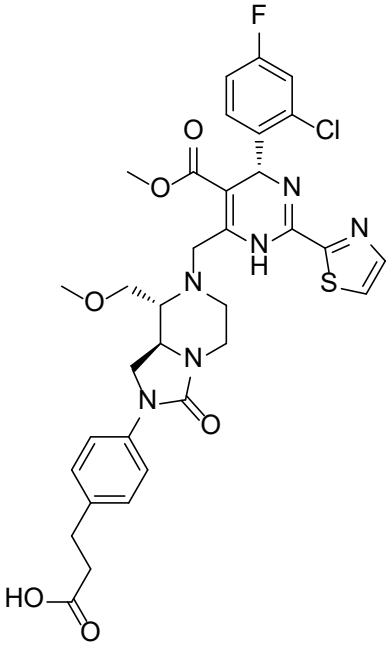

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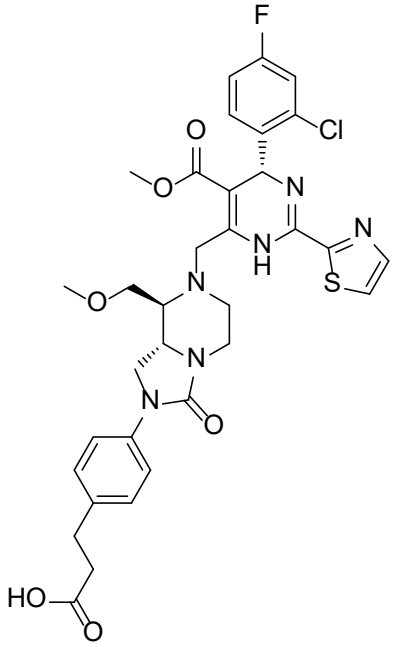
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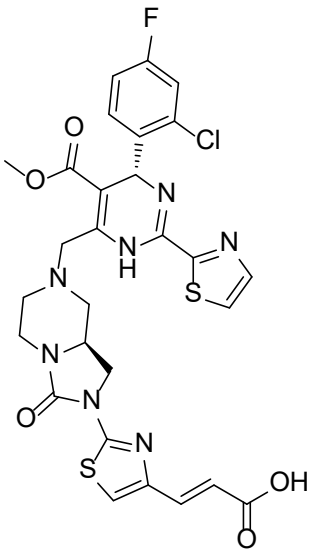
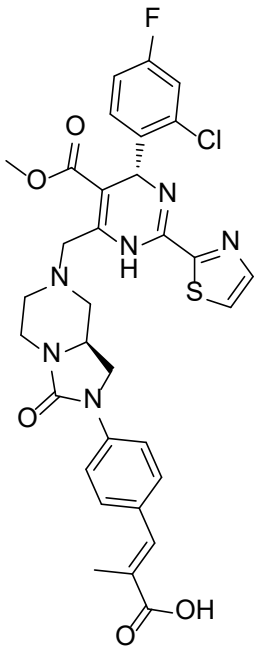
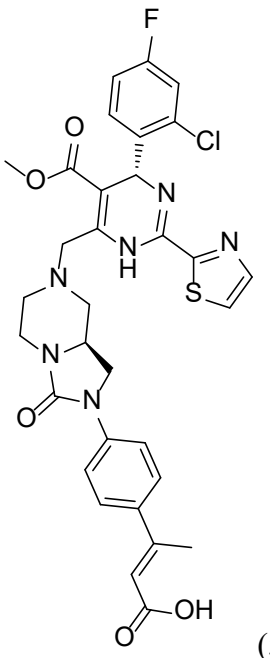
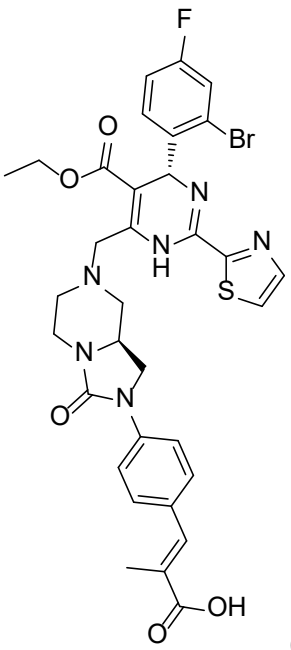
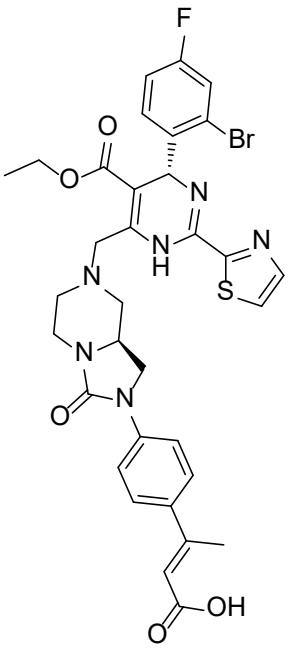
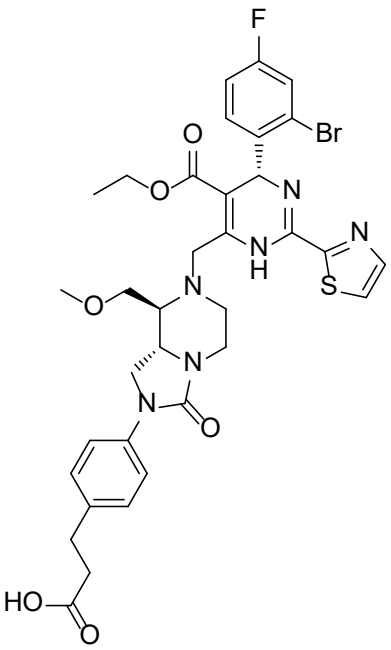
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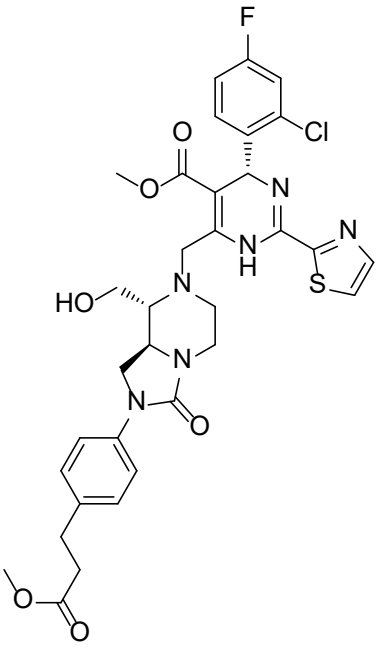


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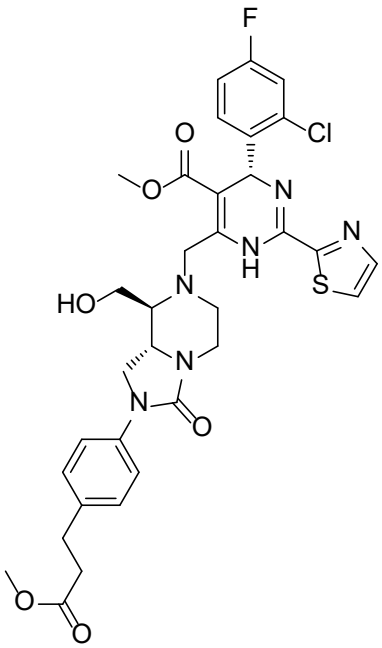


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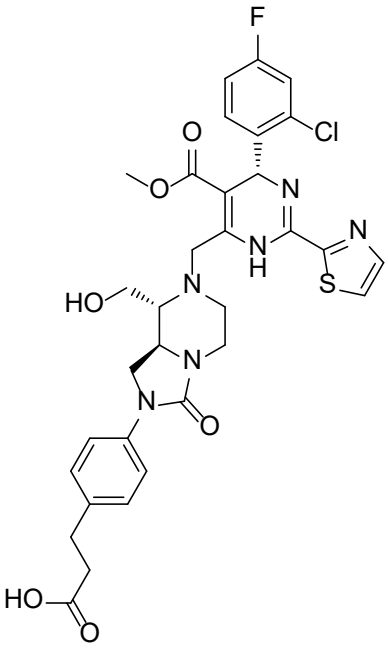

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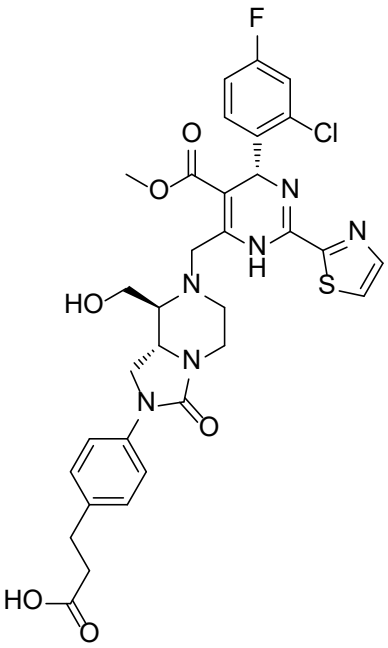
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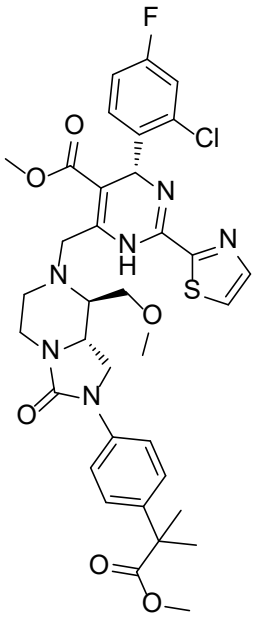
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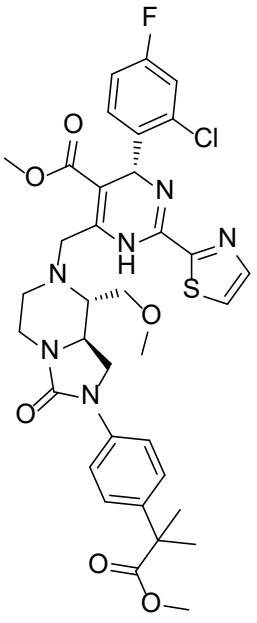
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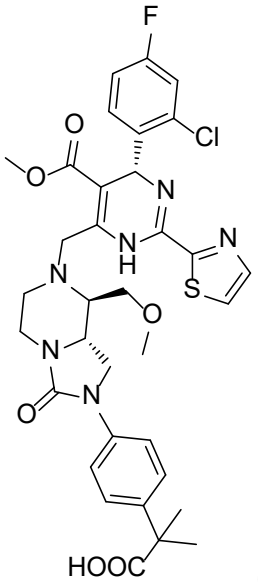
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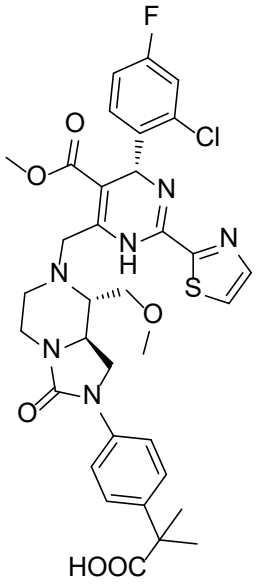
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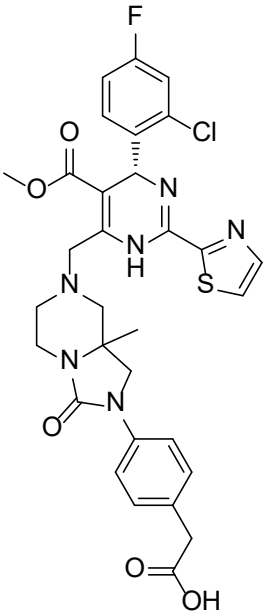
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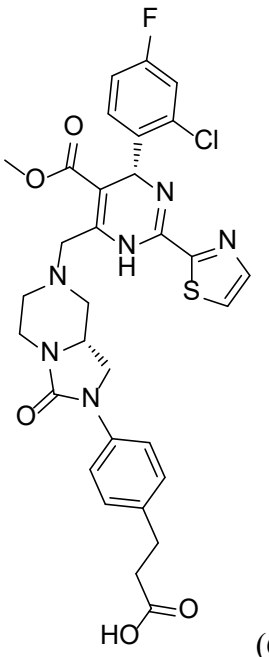
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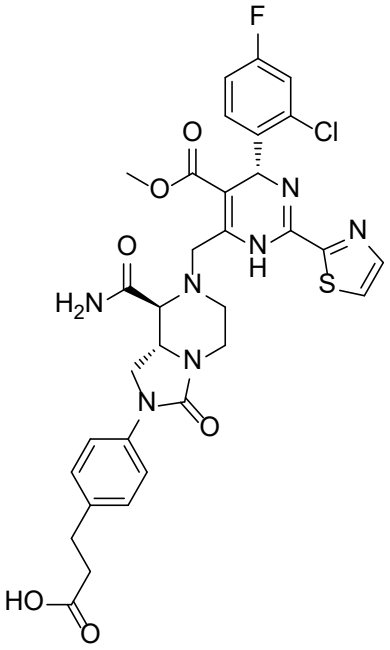
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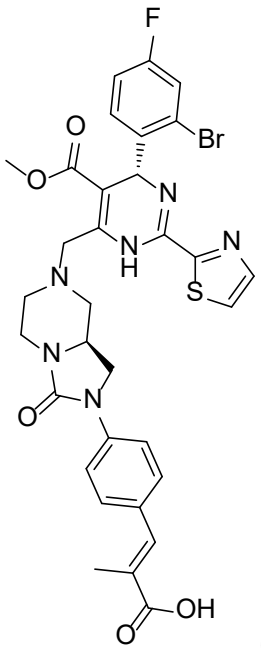
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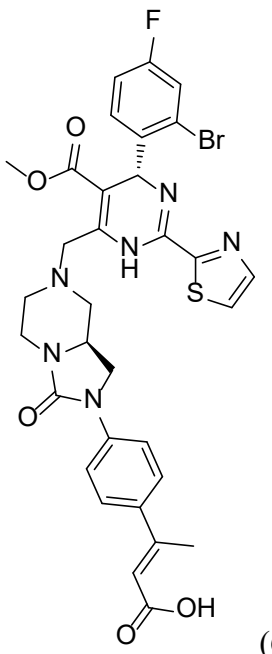
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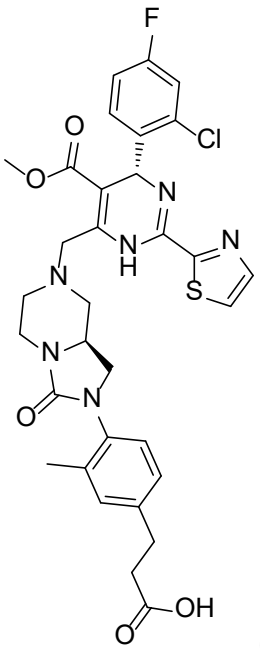
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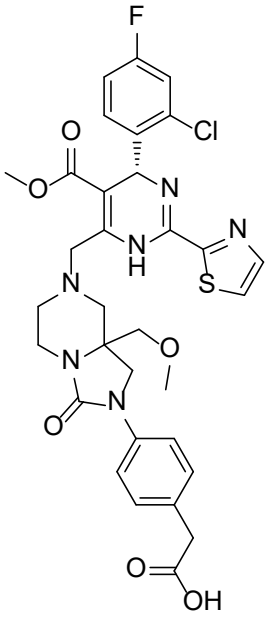
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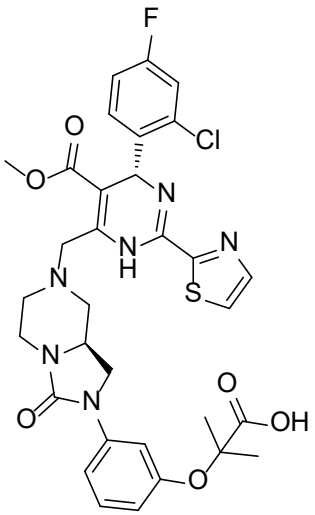
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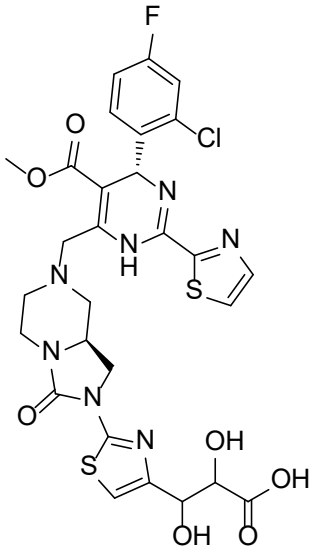
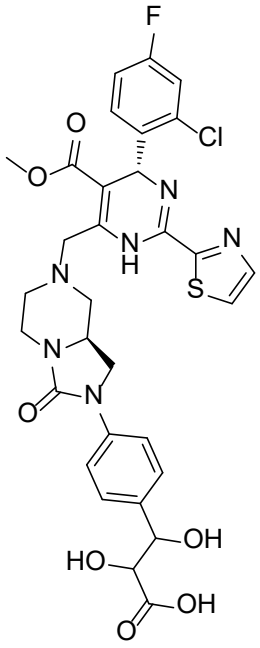
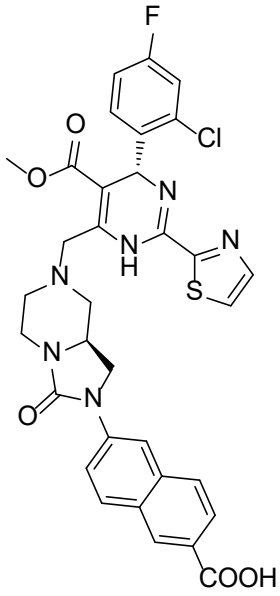
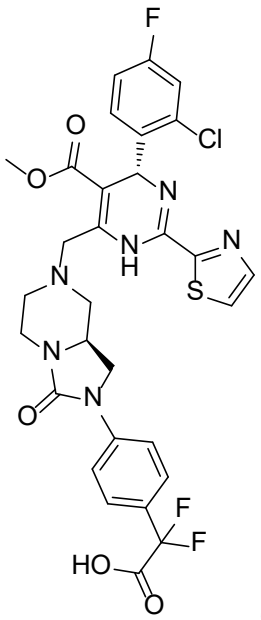
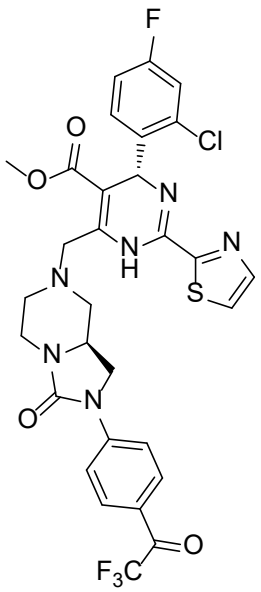
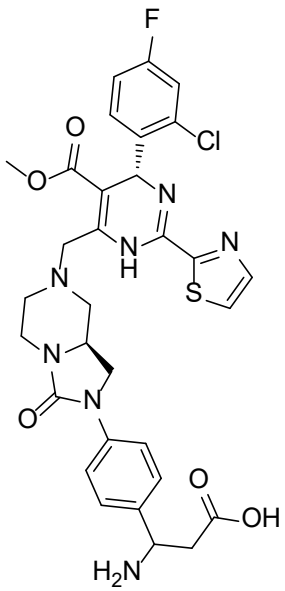
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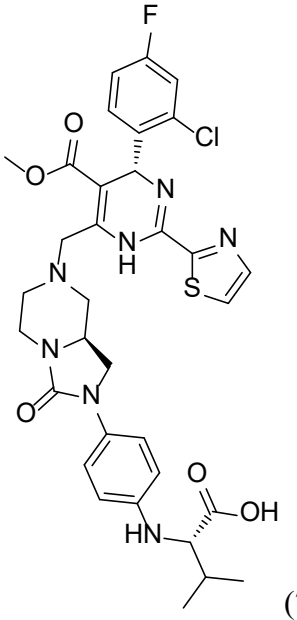
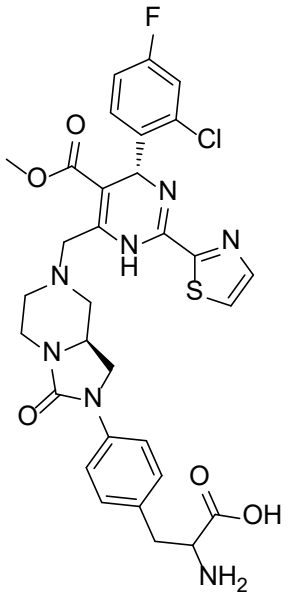
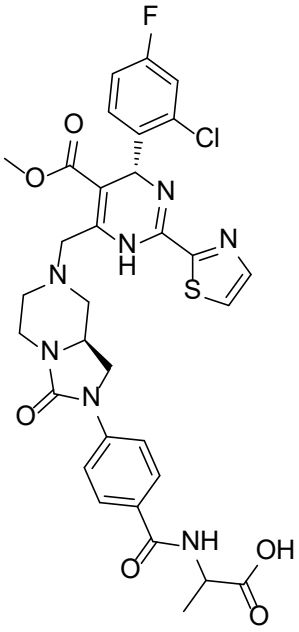
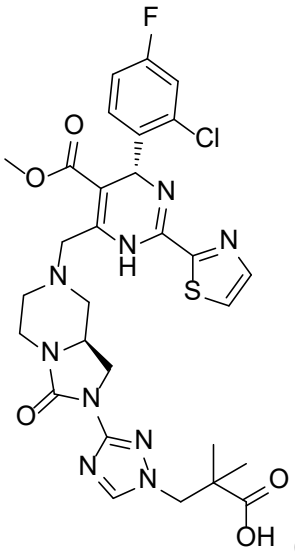
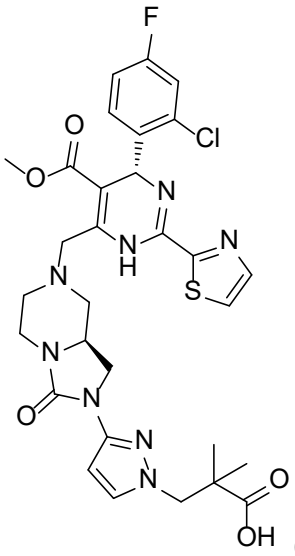


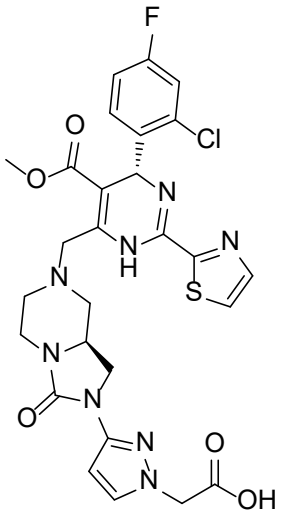
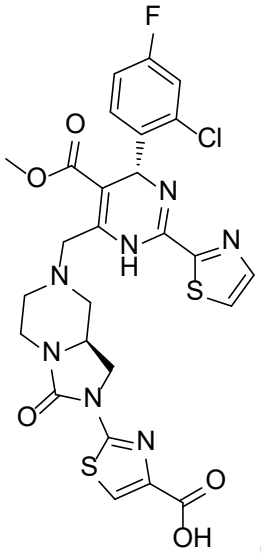
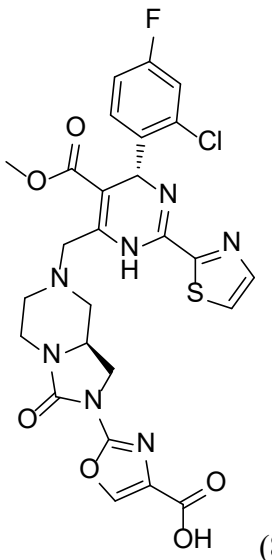
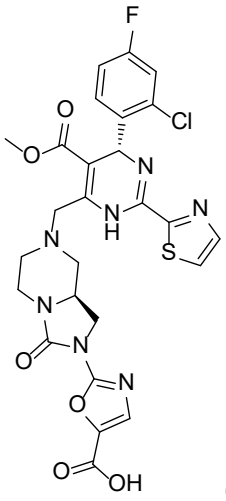
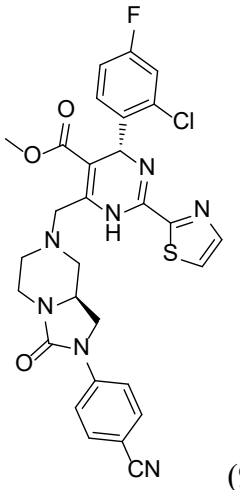
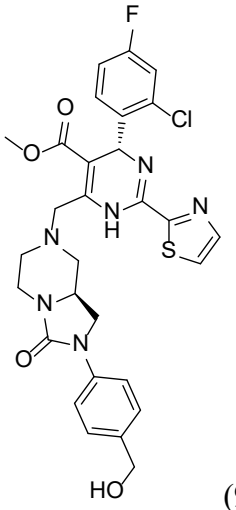
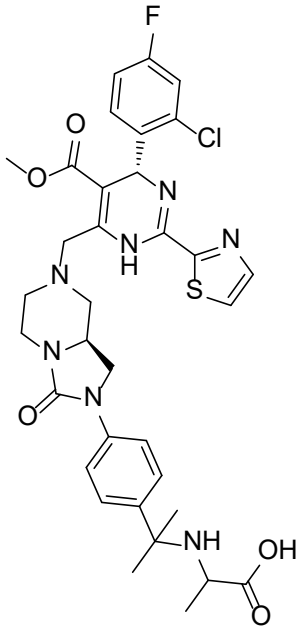
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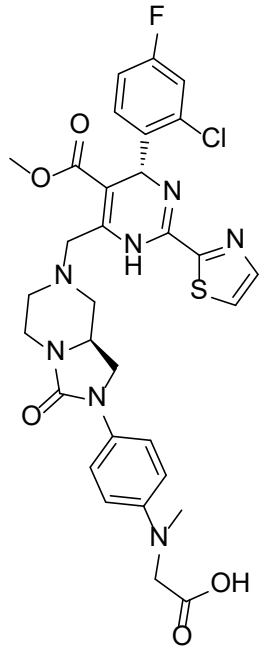


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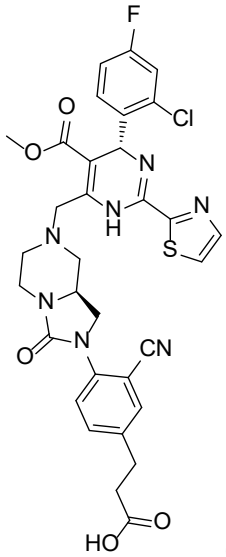

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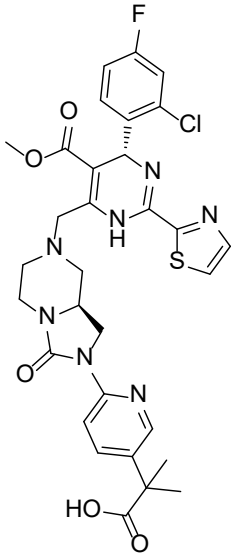

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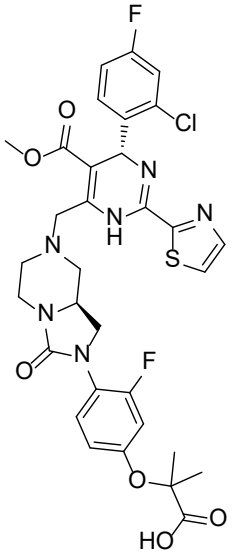
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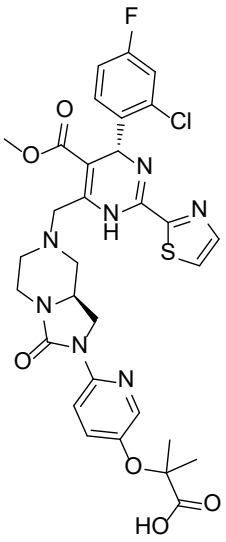
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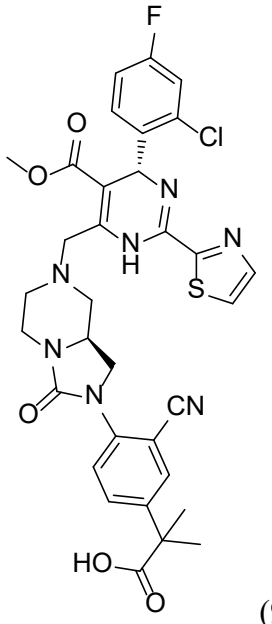
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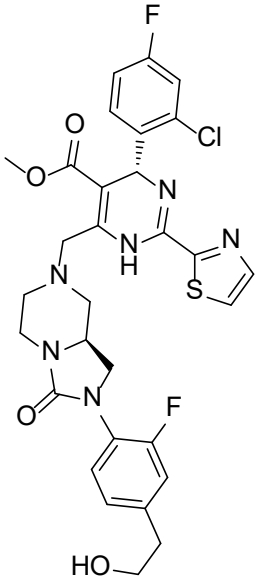
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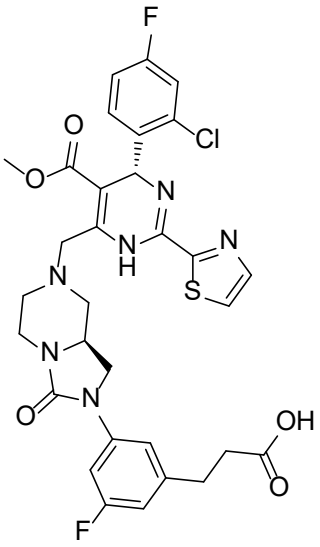
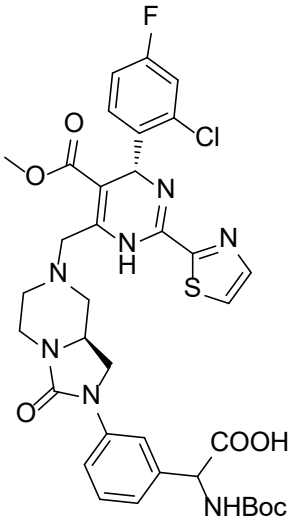
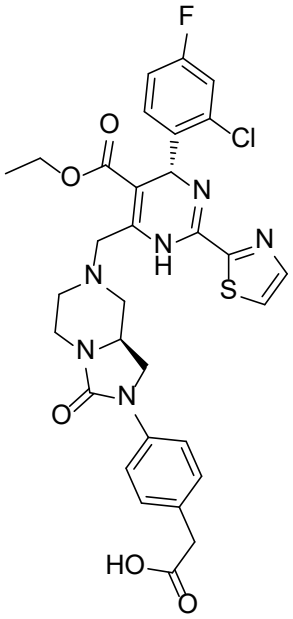


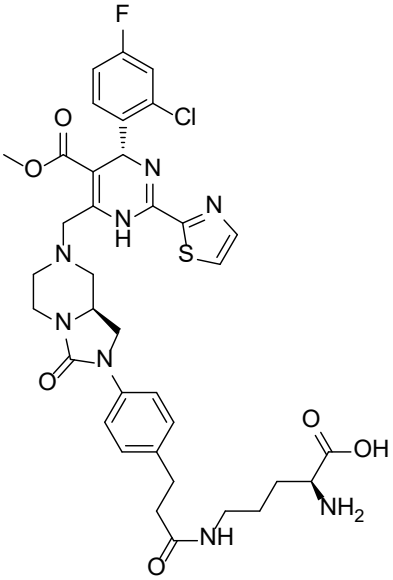
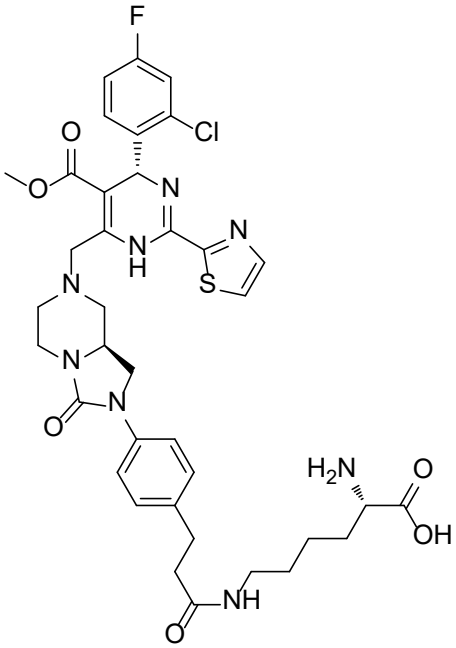
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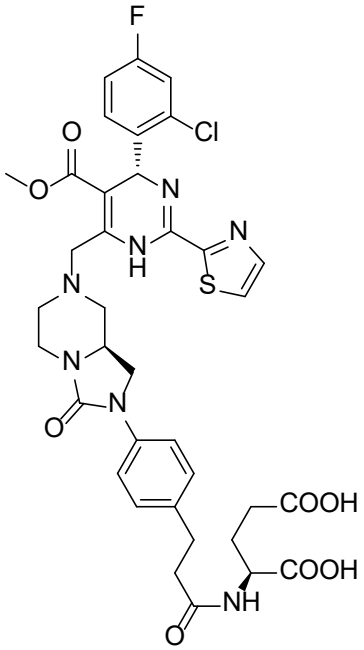


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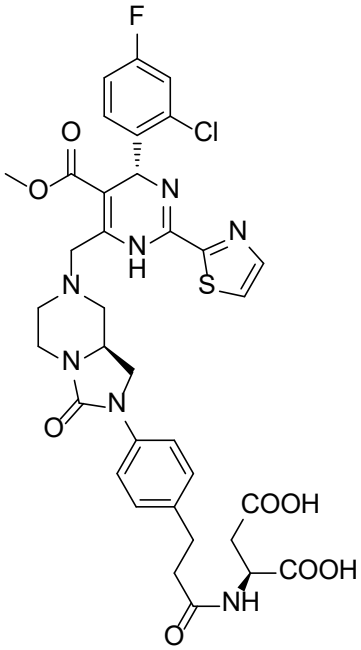


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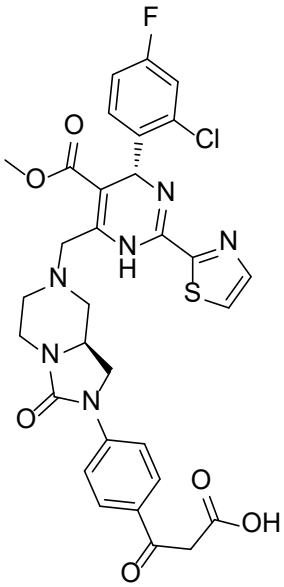
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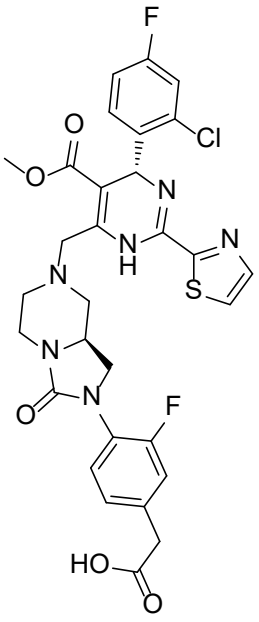


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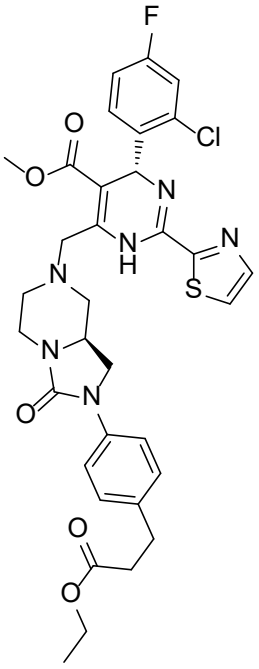


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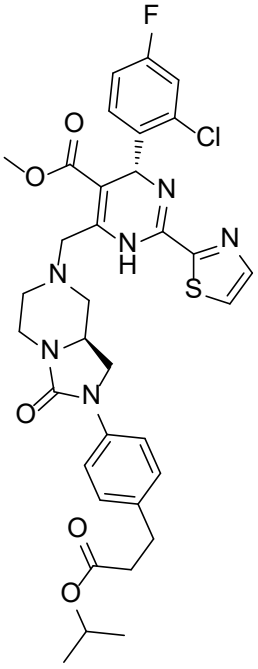




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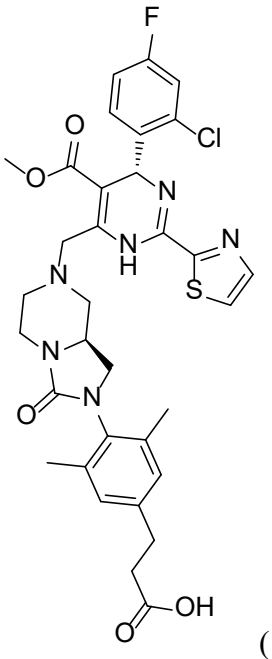


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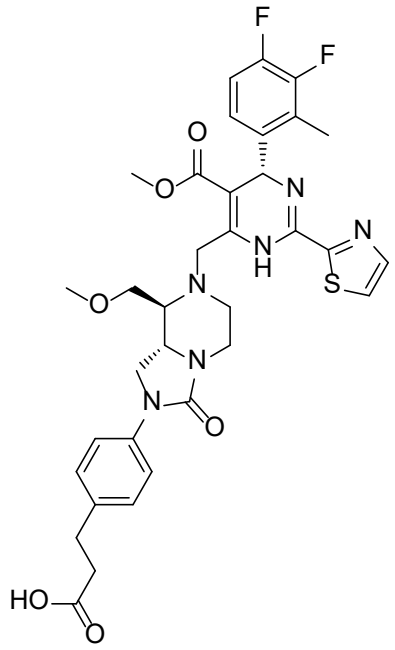


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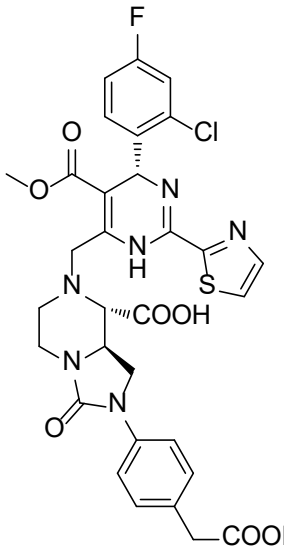
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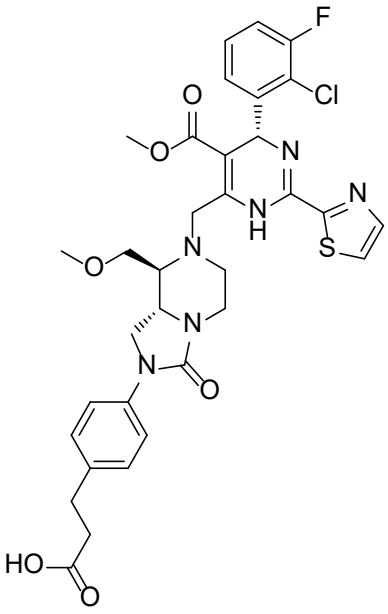
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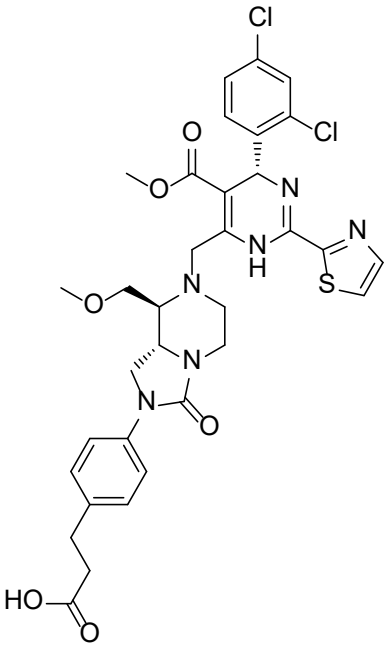
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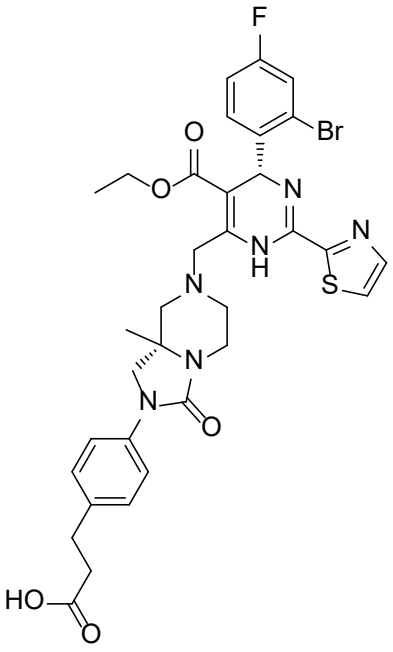
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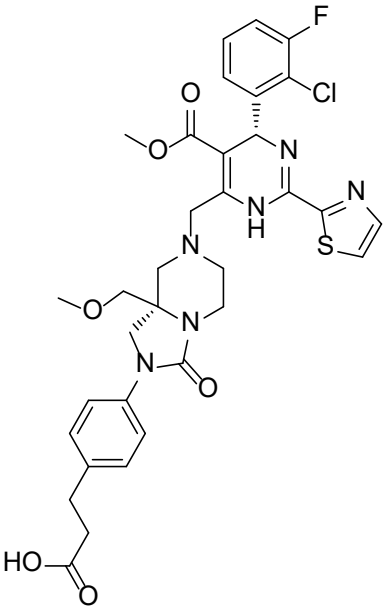
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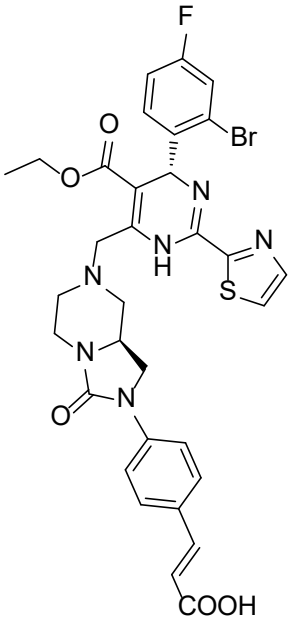
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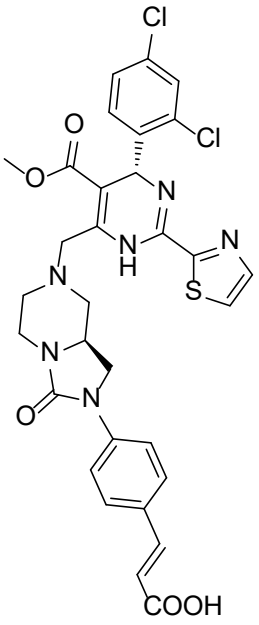
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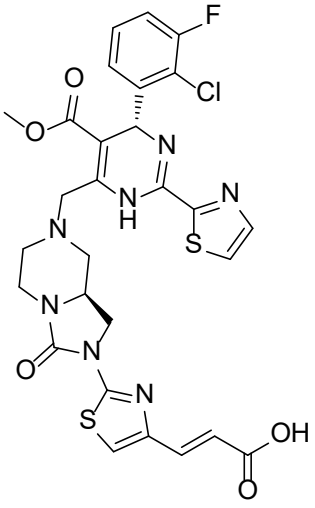
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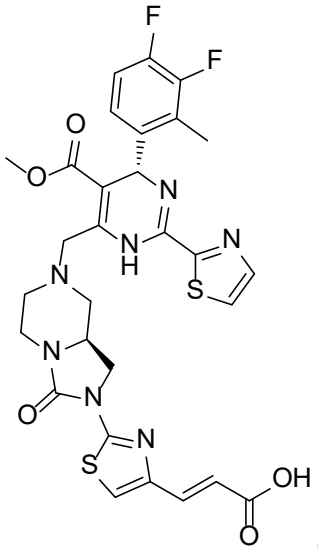
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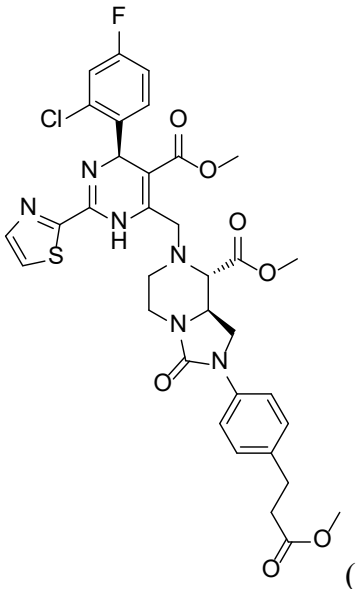
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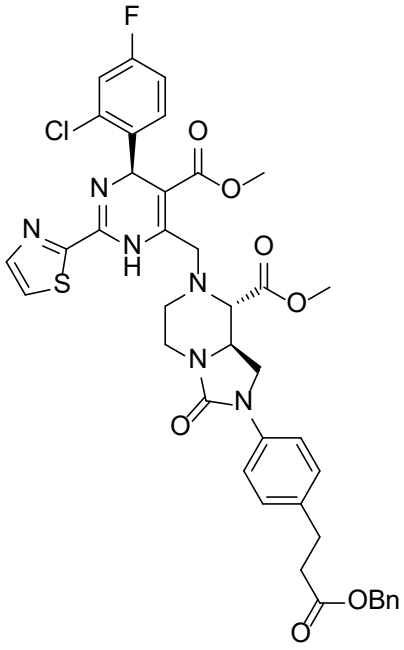
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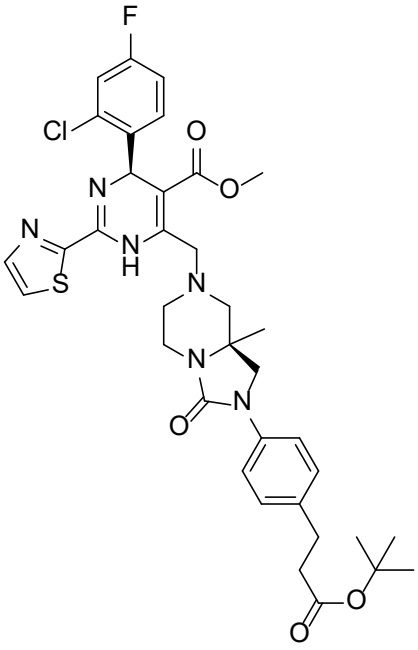
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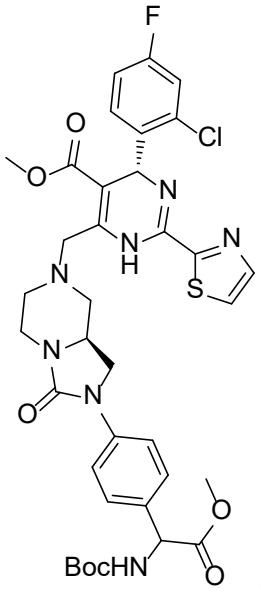
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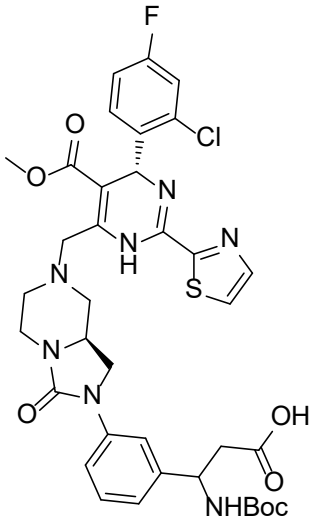
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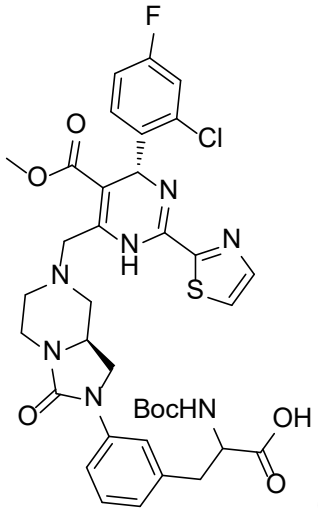
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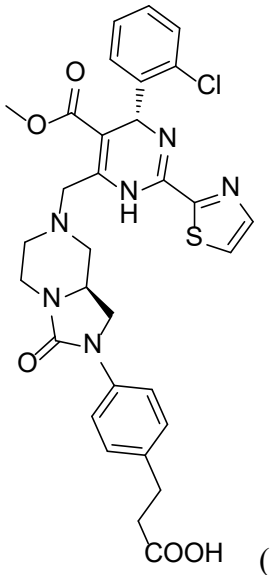
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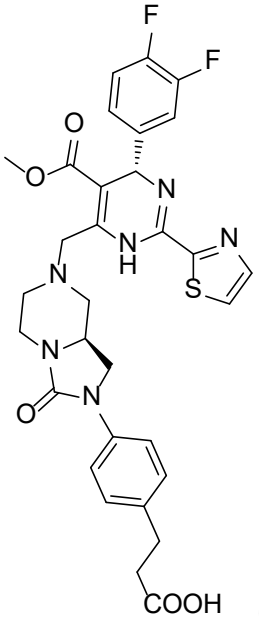
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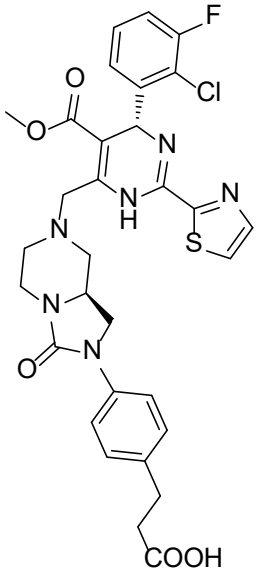
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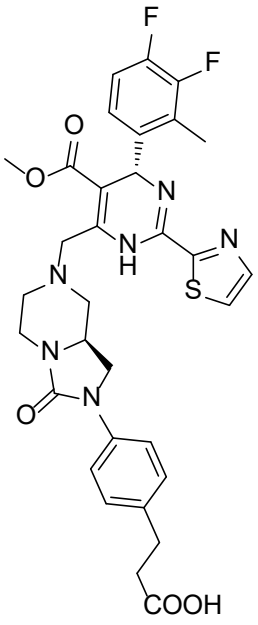
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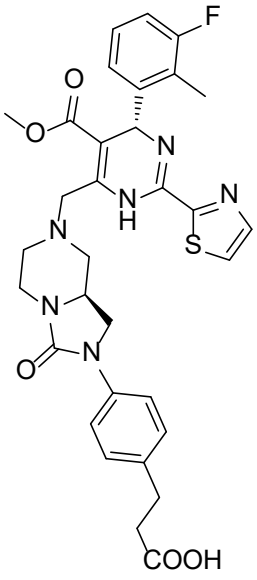


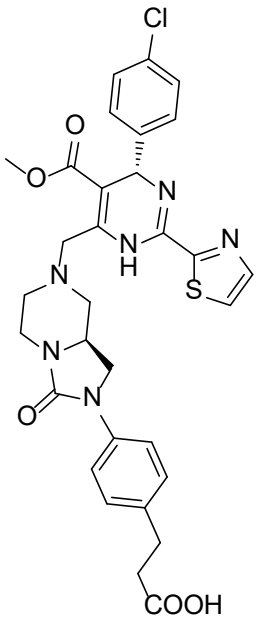
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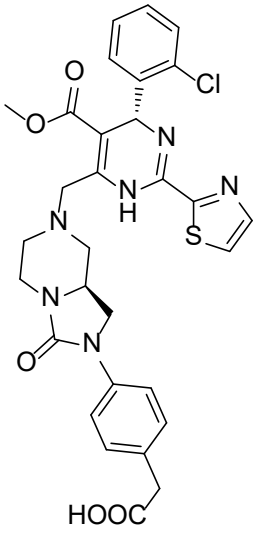


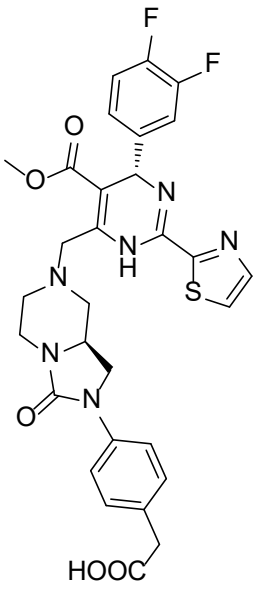
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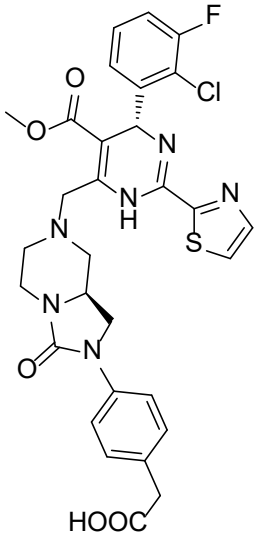


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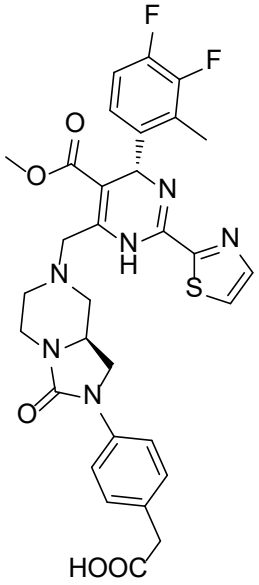
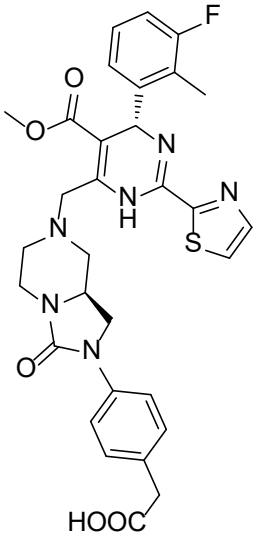
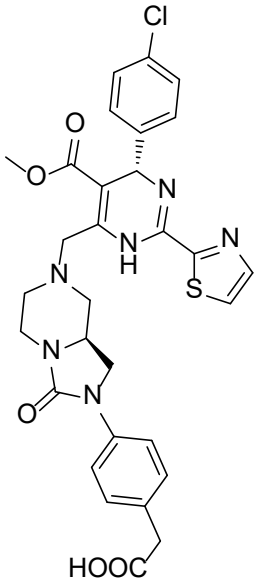
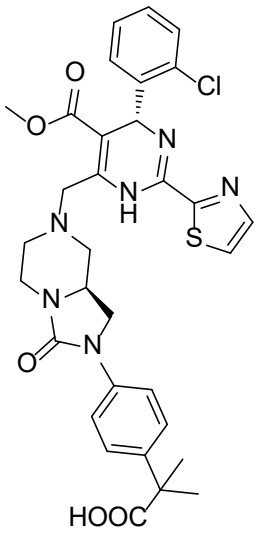
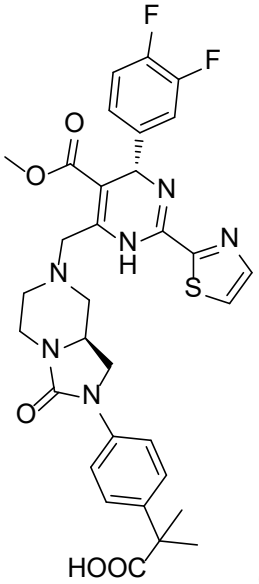
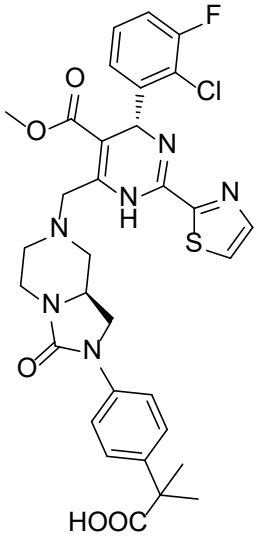
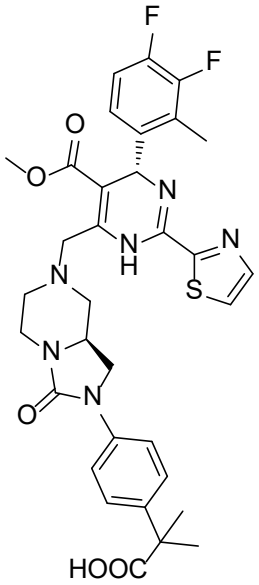
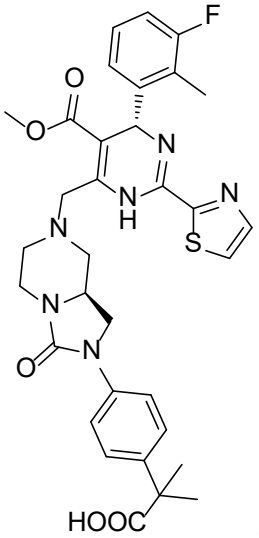
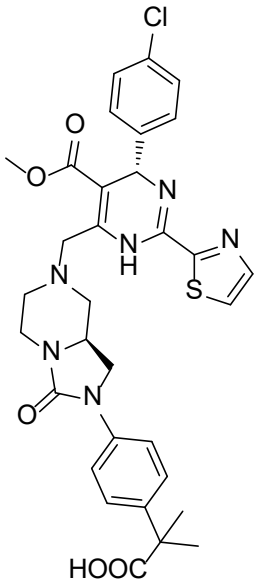
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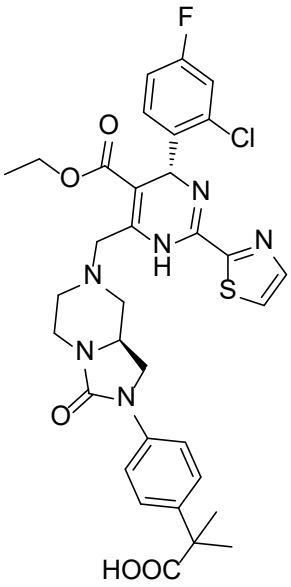
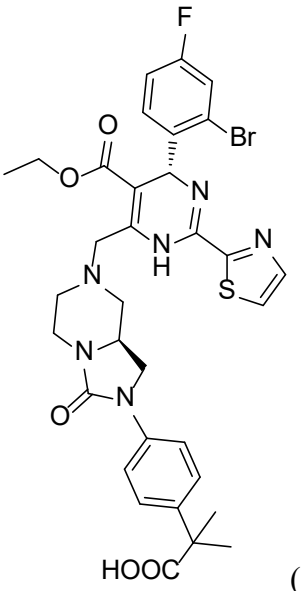
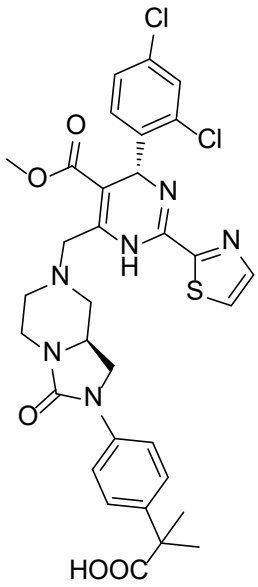
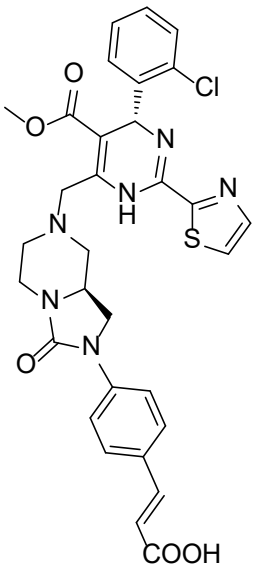
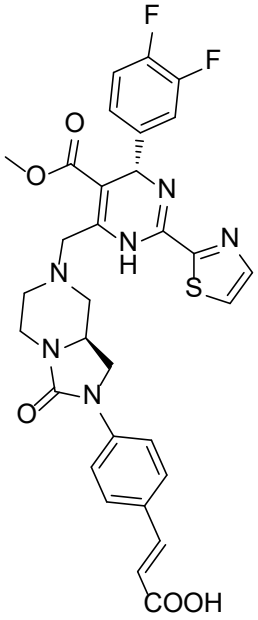
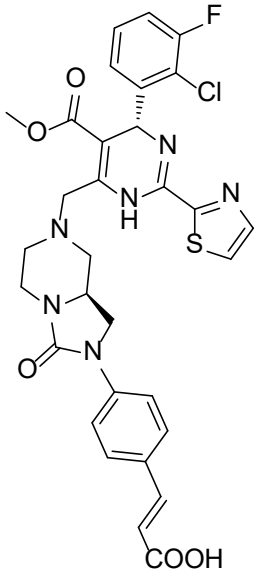
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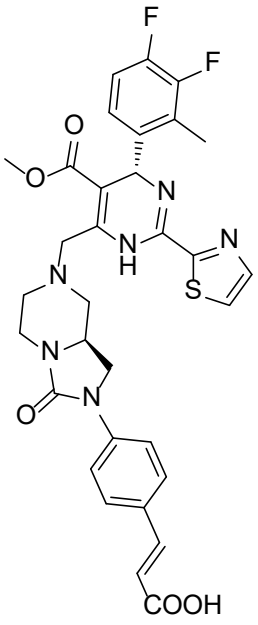
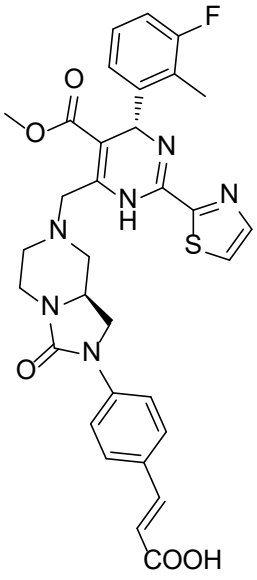
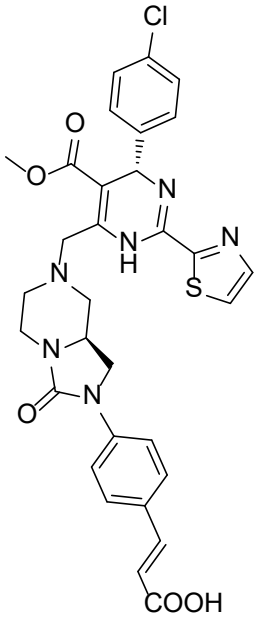
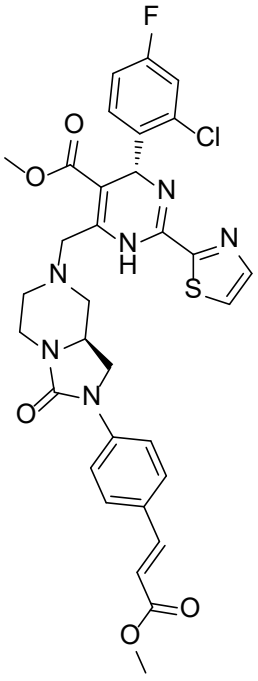
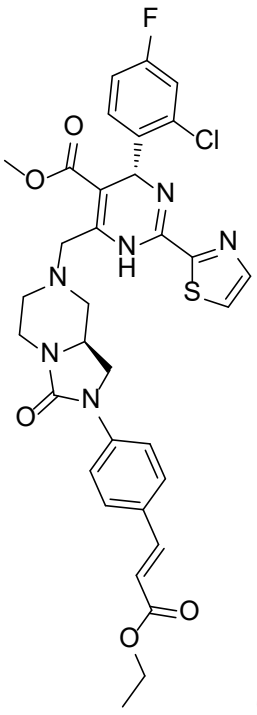
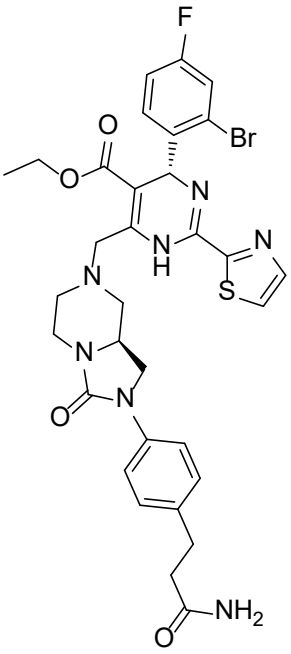
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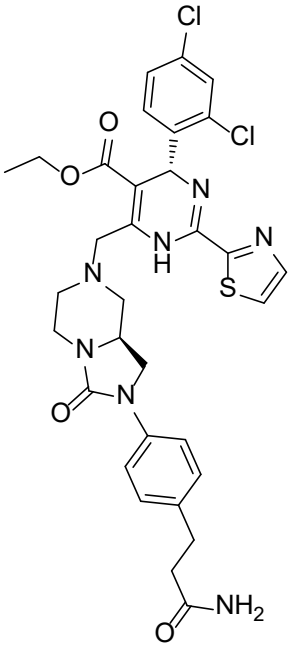
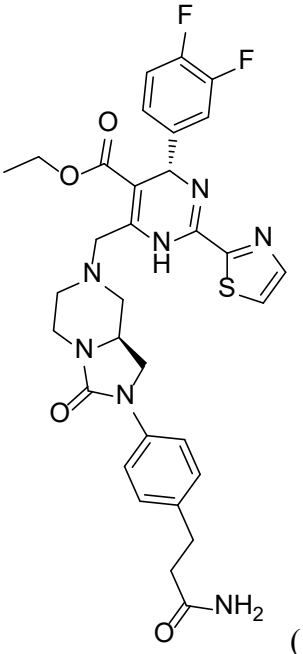
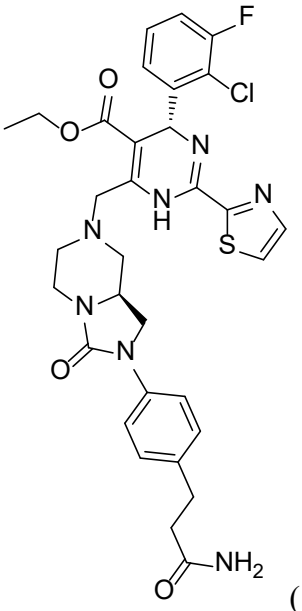
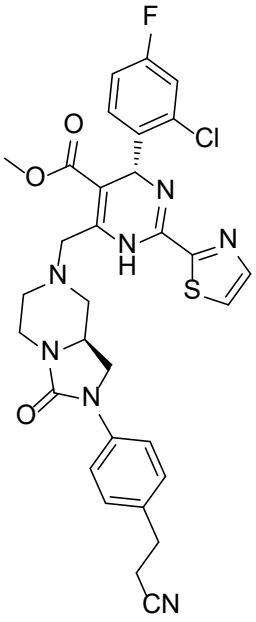
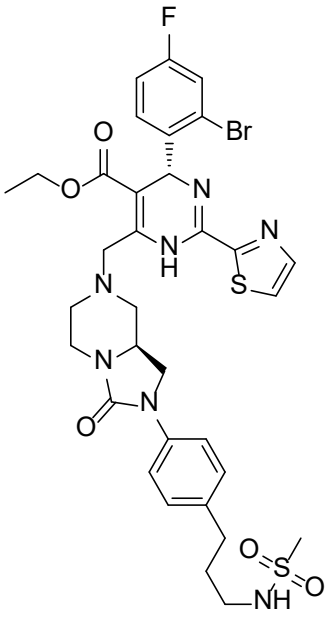
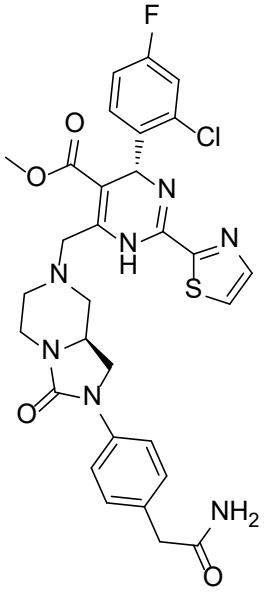
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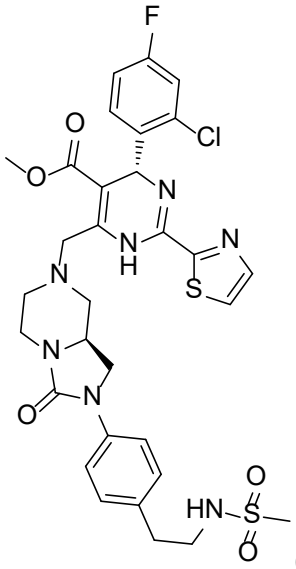
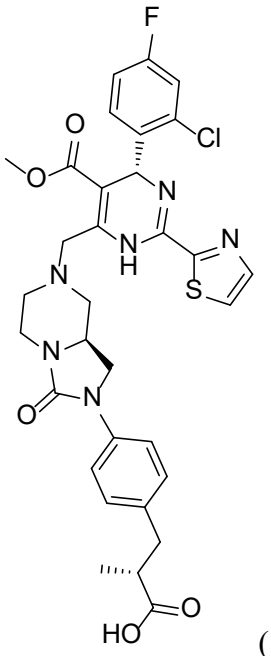
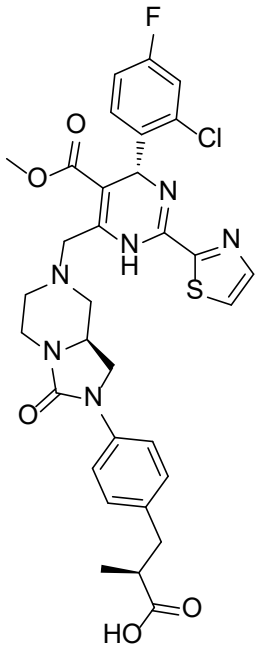
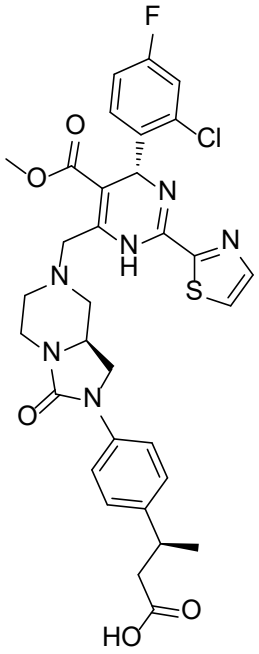
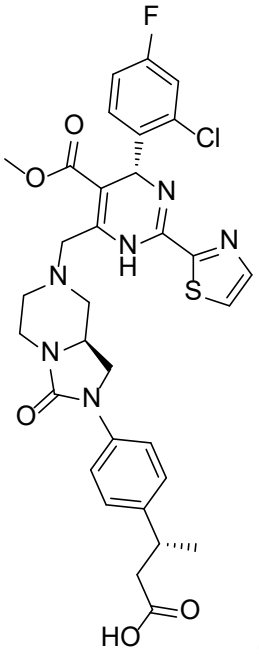
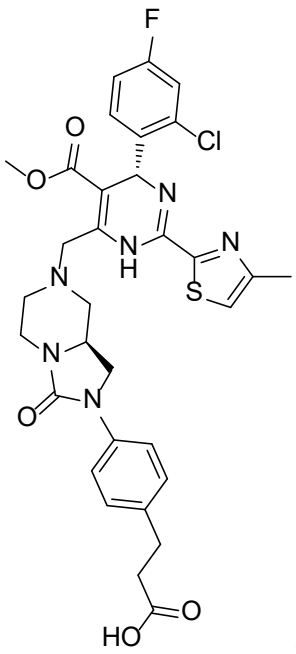
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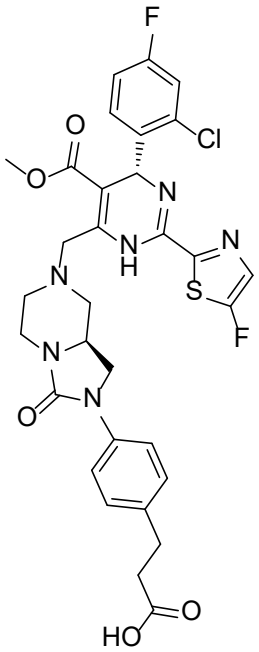

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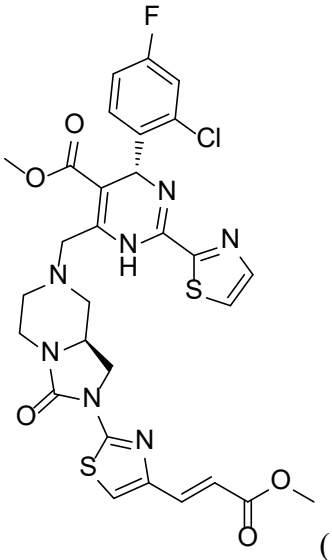

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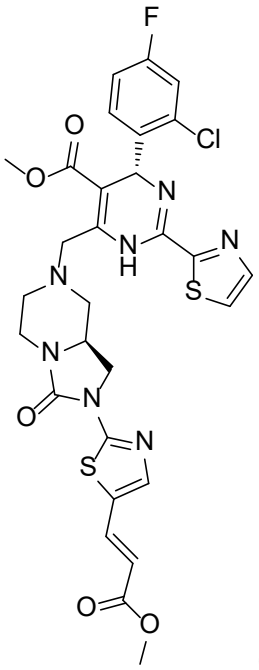

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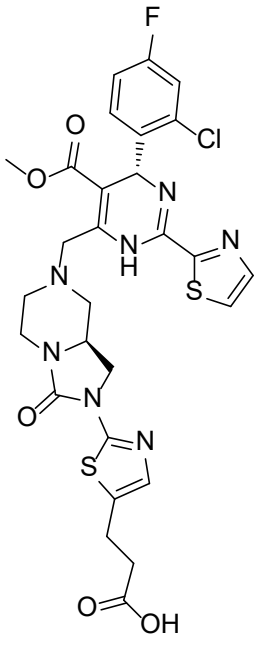
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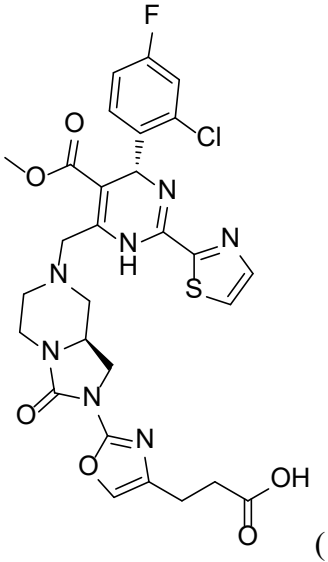
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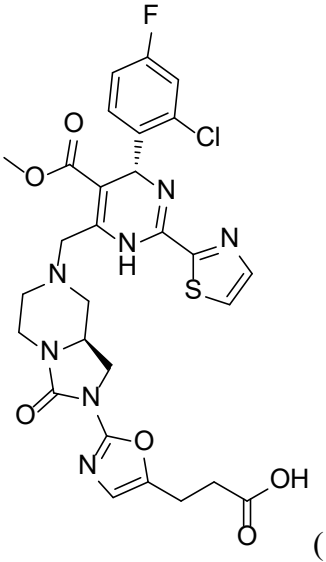
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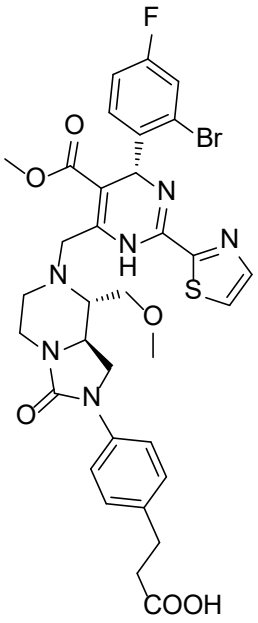
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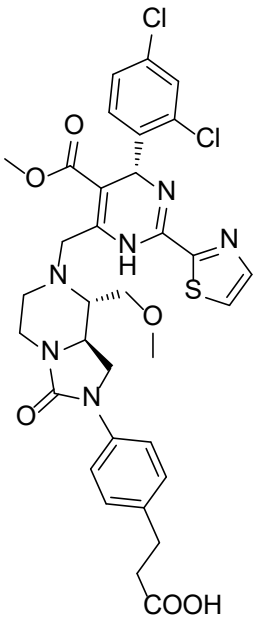


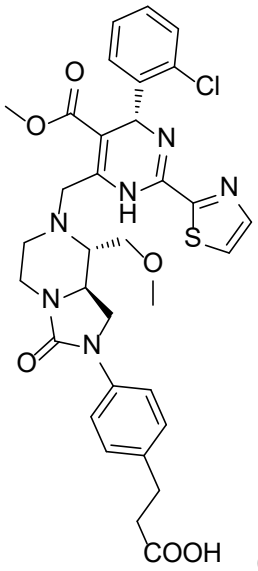
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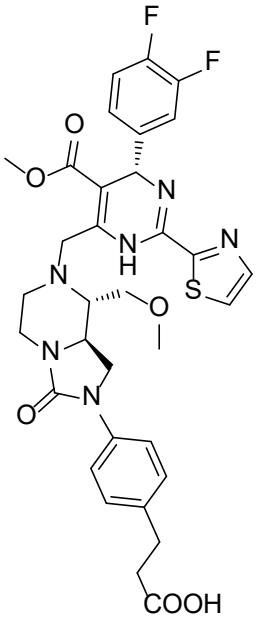


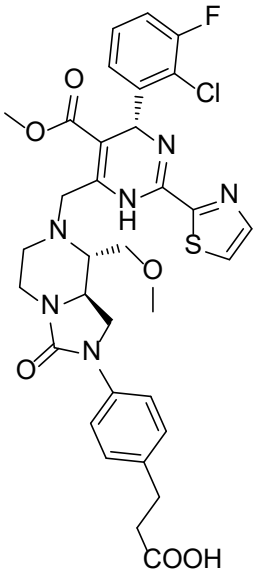
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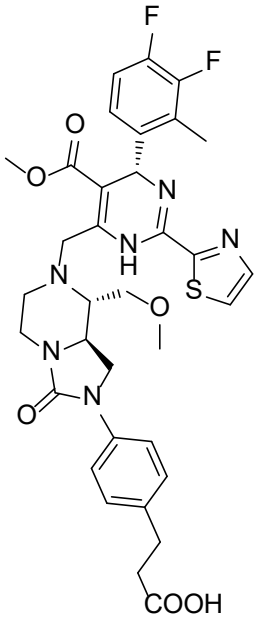


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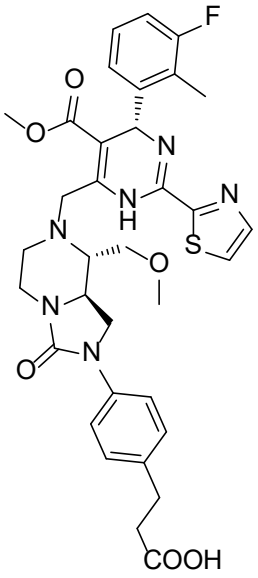
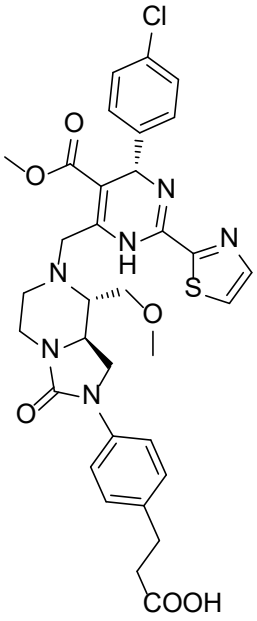
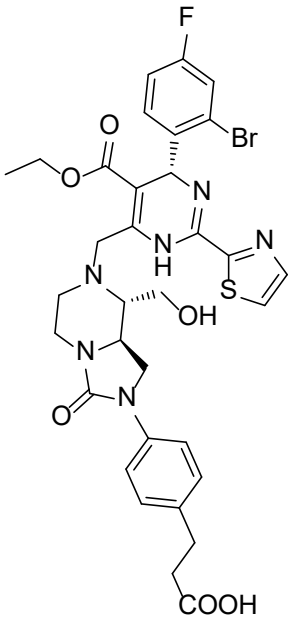
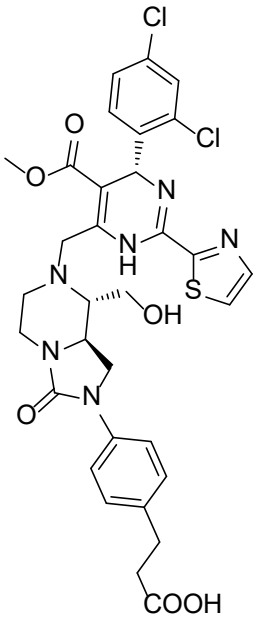
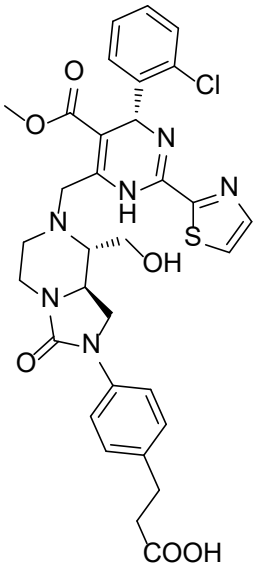
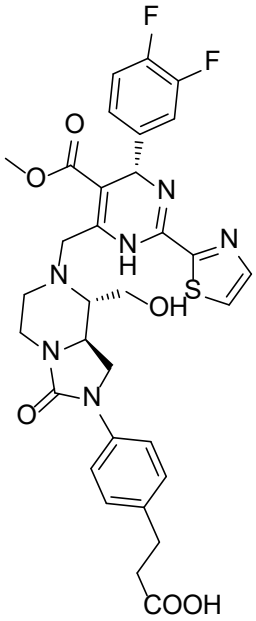
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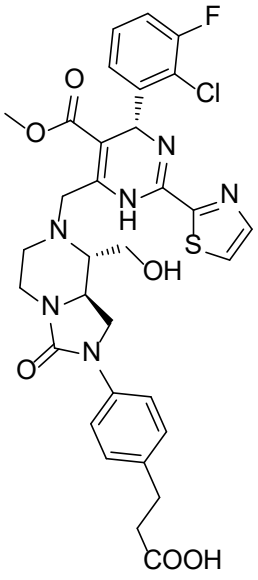
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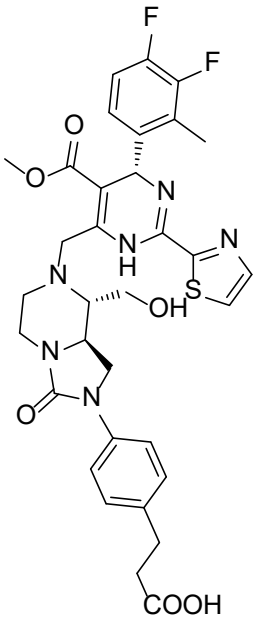
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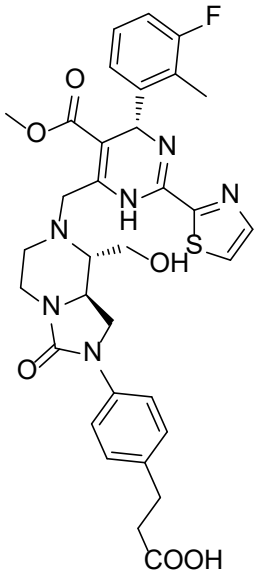
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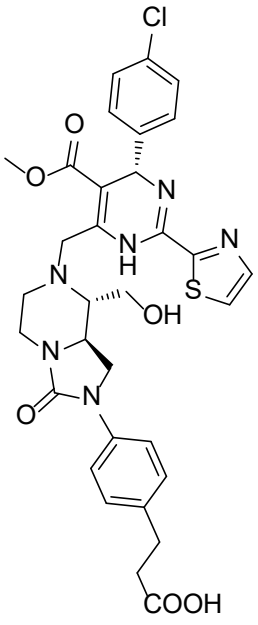
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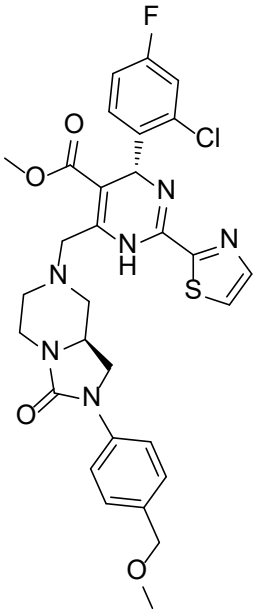

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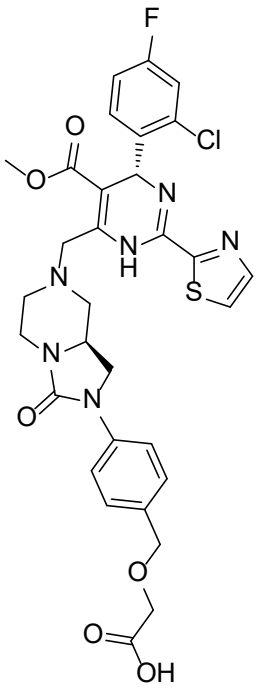


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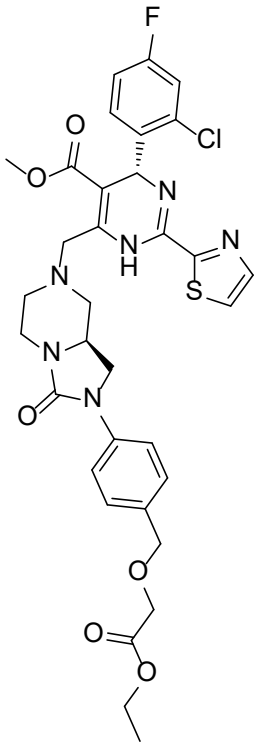
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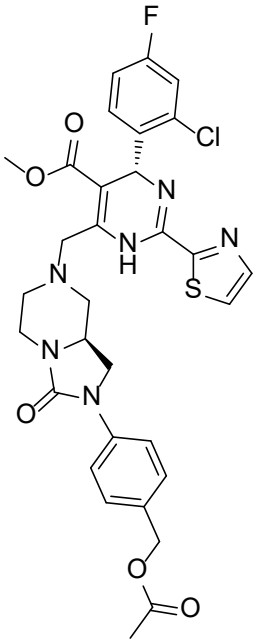
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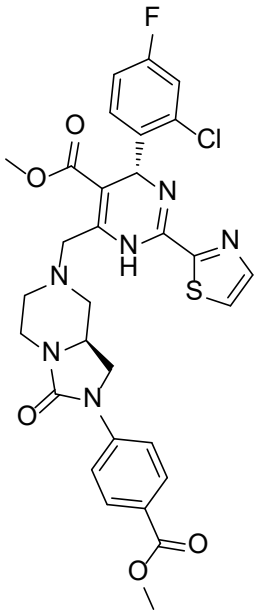
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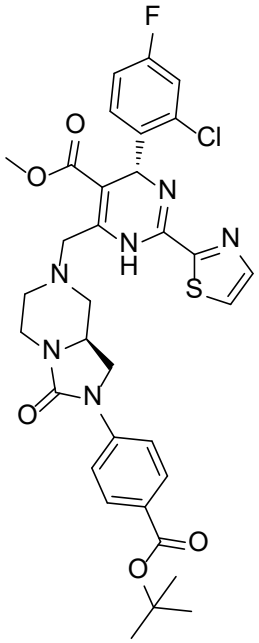
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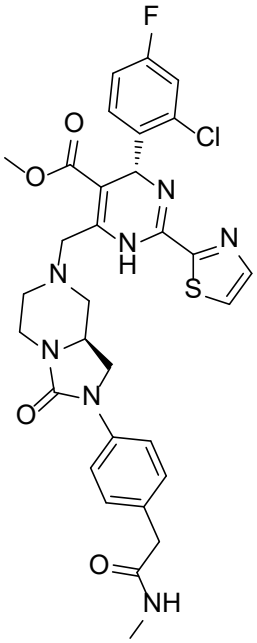
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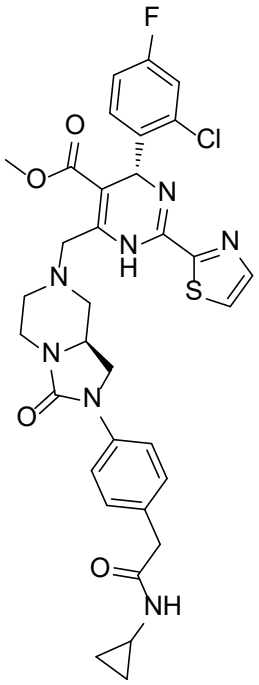
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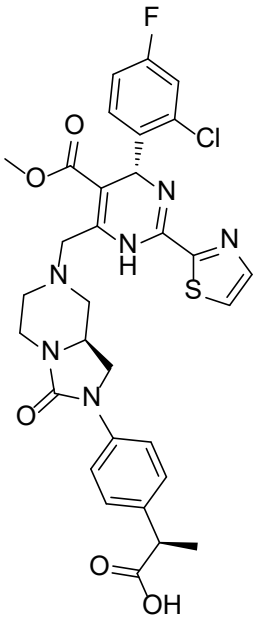
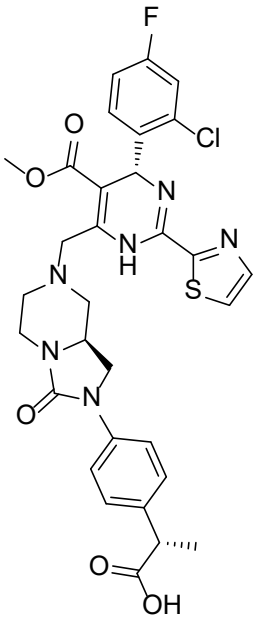
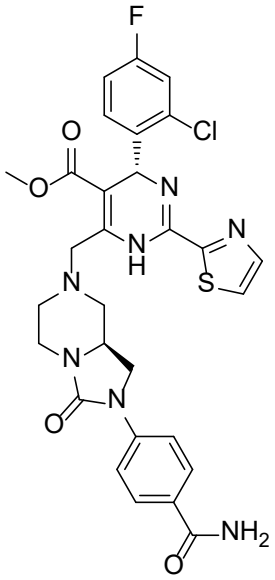
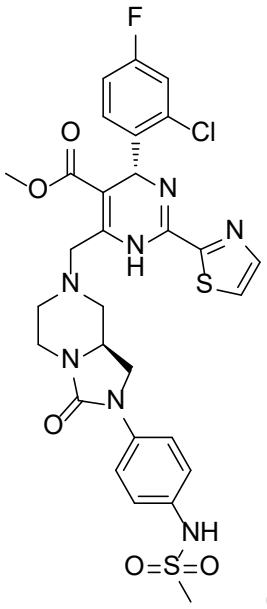
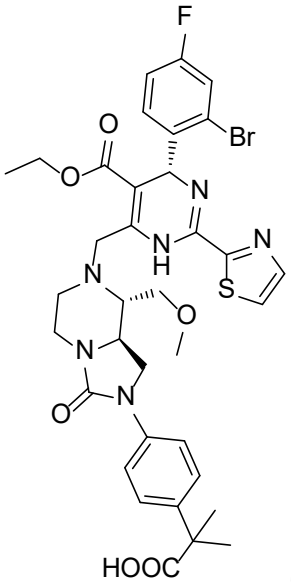
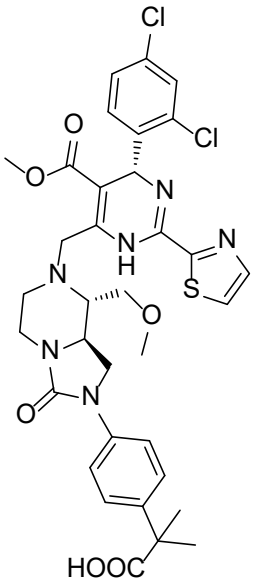
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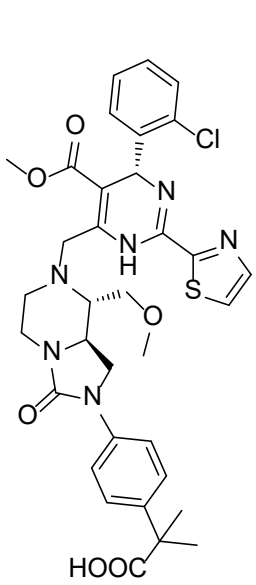


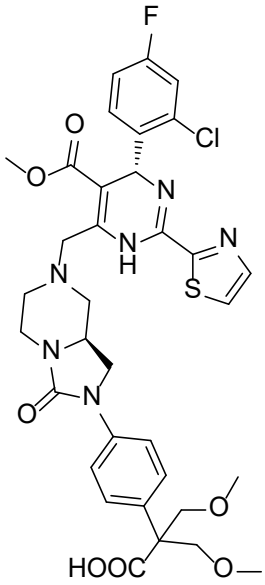
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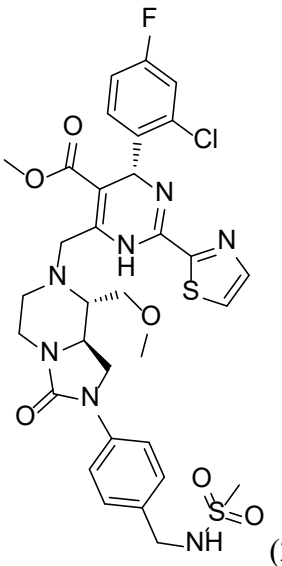


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(212),

or a stereoisomer, a tautomer, an *N*-oxide, a solvate, a metabolite, a pharmaceutically acceptable salt or a prodrug thereof.

13. A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable adjuvant.

14. The pharmaceutical composition of claim 13 further comprising other anti-HBV drug, wherein the other anti-HBV drug is an HBV polymerase inhibitor, immunomodulator or interferon.

15. The pharmaceutical composition of claim 14, wherein the other anti-HBV drug is lamivudine, telbivudine, tenofovir, entecavir, adefovir dipivoxil, alfaferone, alloferon, celmoleukin, clevudine, emtricitabine, famciclovir, feron, hepatect CP, intefen, interferon α-1b, interferon α, interferon α-2a, interferon β-1a, interferon α-2, interleukin-2, mivotilate, nitazoxanide, peginterferon alfa-2a, ribavirin, roferon-A, sizofiran, Euforavac, rintatolimod, Phosphazid, Heplisav, interferon α-2b, levamisole, or propagermanium.

16. Use of the compound of any one of claims 1 to 12 or the pharmaceutical composition of any one of claims 13 to 15 in the manufacture of a medicament for treating or lessening a virus disease in a patient, wherein the virus disease is hepatitis B infection or a disease caused by hepatitis B infection.

17. The use of claim 16, wherein the disease caused by hepatitis B infection is hepatic cirrhosis or hepatocellular carcinogenesis.

18. The compound of any one of claims 1 to 12 or the pharmaceutical composition of any one of claims 13 to 15 for use in treating or lessening a virus disease in a patient, wherein the virus disease is hepatitis B infection or a disease caused by hepatitis B infection.

19. The compound or the pharmaceutical composition of claim 18, wherein the disease caused by hepatitis B infection is hepatic cirrhosis or hepatocellular carcinogenesis.